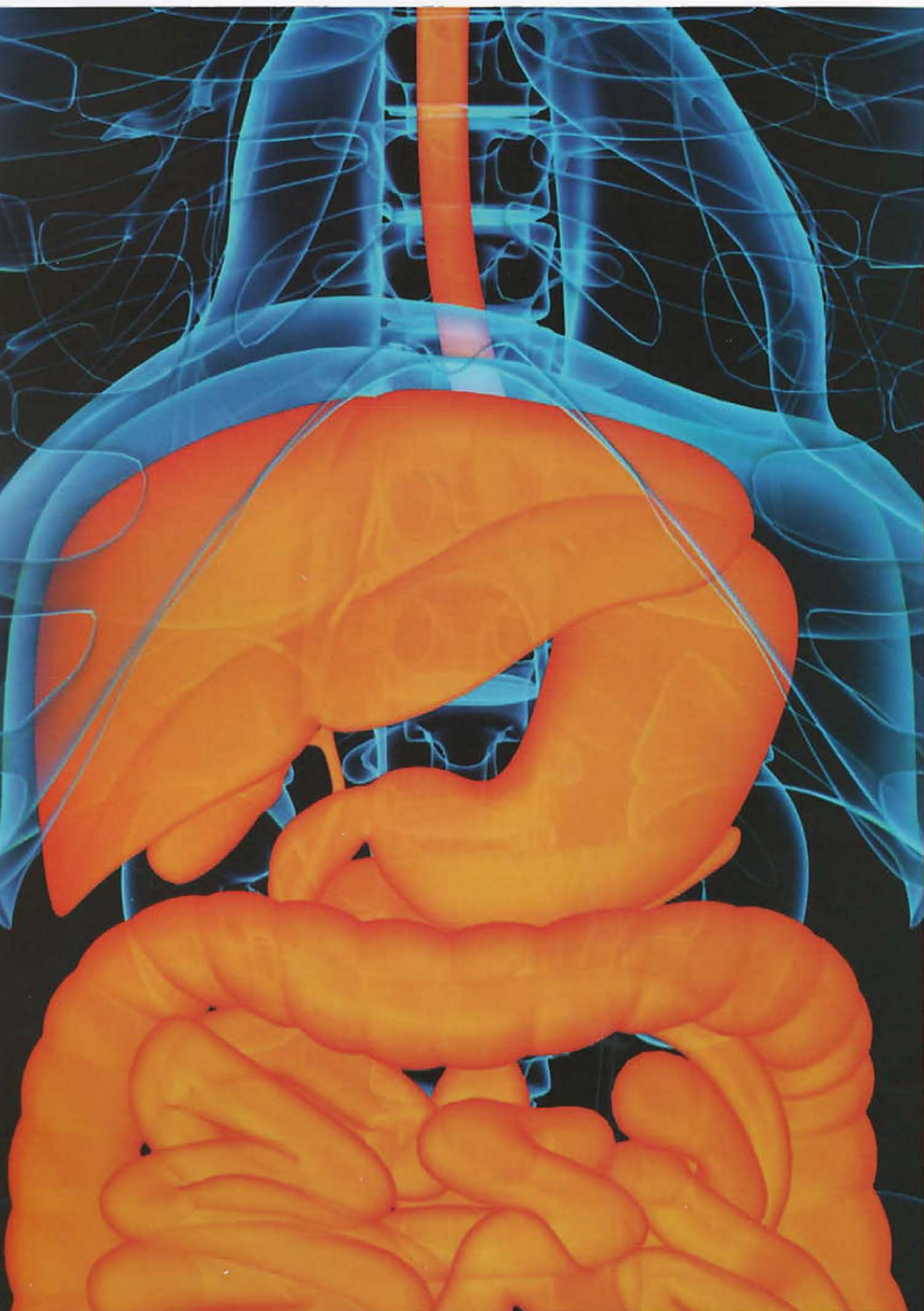


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GASTROENTEROLOGY

By :

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

لَا يُكَلِّفُ اللَّهُ نَفْسًا إِلَّا وُسْعَهَا لَهَا مَا كَسَبَتْ وَعَلَيْهَا مَا اكْتَسَبَتْ رَبَّنَا لَا تُؤَاخِذْنَا إِنْ
نَسِينَا أَوْ أَخْطَأْنَا رَبَّنَا وَلَا تَحْمِلْ عَلَيْنَا إَصْرًا كَمَا حَمَلْتَهُ عَلَى الَّذِينَ مِنْ قَبْلِنَا رَبَّنَا وَلَا
تَحْمِلْنَا مَا لَا طَاقَةَ لَنَا بِهِ وَاعْفُ عَنَّا وَاعْفِرْ لَنَا وَارْحَمْنَا أَنْتَ مَوْلَانَا فَانصُرْنَا عَلَى
الْقَوْمِ الْكَافِرِينَ

صدق الله العظيم

سورة البقرة (آية 286)

Preface

- *First and foremost, thanks are due to **ALLAH**, to whom I relate any success in achieving any work in my life.*
- *Great thanks to those who helped me, and greater thanks to those who try to break my wings as they make me more able to fly.*
- *My thanks are extended to all my medical students whom I produce this series "**In Capsule Series**" to obtain a higher degree in internal medicine by a simple effort.*
- *Finally, I wish to thank all members of My Family, my colleagues , my Friends and even all my patients for their continuous help, encouragement and support.*

Ahmed Mowafy

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LIVER

Introduction:

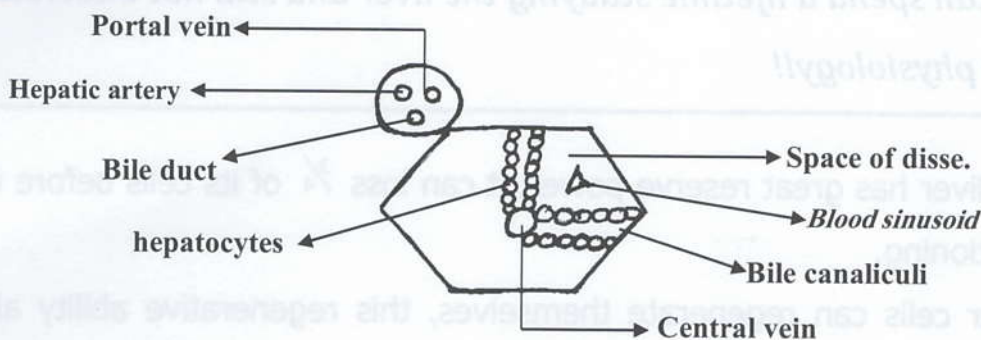
- Liver is the largest & heaviest internal organ in the body (1500 gm).
- The liver is the **main industrial centre** of the body it's involved with almost all the biochemical pathways that allow growth, supply nutrients, provide energy & aid reproduction.
- Liver cells (*hepatocytes*) go thousands of complex biochemical reactions every second in order to perform these function.
- In brief, *you can't **live** without **liver**.*

Anatomy:

- The liver is located behind the lower ribs, right below diaphragm on the right side of abdomen separated superiorly by falciform ligament & inferiorly by ligamentum teres.
- Right lobe is much larger & has 2 additional lobes (*caudate & quadrate*)

Histology:

- **Hepatic lobule:** is the basic unit for liver function:



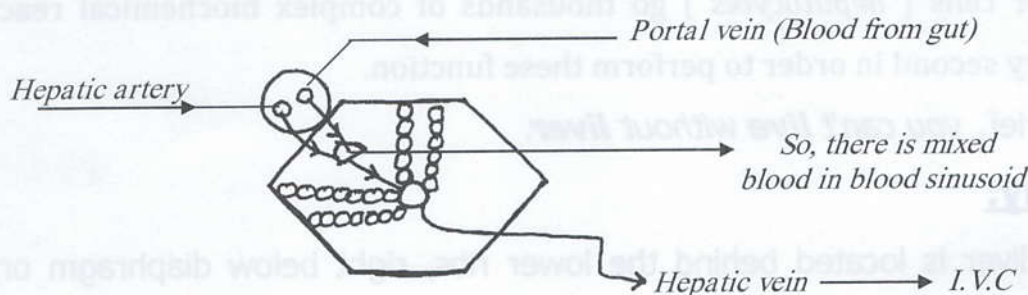
- The walls of the sinusoids consist of endothelial & macrophage cells known as "*Kupffer cells* "
- These kupffer cells phagocytes bacteria, viruses & immune complexes.

Blood Supply of the liver : 25% of the resting cardiac output

- Liver has double blood Supply :
 - i- Hepatic artery (1/3) → carries oxygenated blood.
 - ii- Portal vein (2/3) → bringing blood from the intestine & spleen.

Venous drainage:

Drainage is via the hepatic veins into the inferior vena cava.

Portal circulation:**Liver functions :** (Details : [see liver function tests](#))

- i. Liver is very important in proper protein, carbohydrate & fat metabolism.
- ii. Making bile.
- iii. Detoxification: filtering of the blood.

You can spend a lifetime studying the liver and still not understand all of its physiology!!

- The liver has great reserve power, it can loss $\frac{3}{4}$ of its cells before it stops functioning.
- Liver cells can regenerate themselves, this regenerative ability allows a diseased liver to return to normal function in some cases. Very few organs in the body have this ability.
- So, this great reserve power means that diseases that affect the liver show no symptoms in early stages & this makes the prognosis worse.

Rule of 6 in Hepatology :

1. Pathogenesis (Etiology) of Ascites in hepatic patient 6 items.
2. Treatment of Ascites in hepatic patient. 6 items
3. Precipitating factors of hepatic encephalopathy..... 6 items.
4. c/p of hepatic encephalopathy (pre coma).....6 items.
5. Treatment of hepatic encephalopathy..... 6 items.
6. c/p of portal hypertension 6 items
7. Complications of portal hypertension..... 6 items.
8. Investigations of portal hypertension..... 6 items.
9. Treatment of portal hypertension (esophageal varices)..... 6 items.
10. Prevention of esophageal varices..... 6 items.
11. Complications of hepatitis 6 items.
12. Investigations of hepatitis..... 6 items.
13. Treatment of acute hepatitis 6 items.
14. Indications of liver transplantation 6 items.
15. Complications of liver transplantation 6 items.
16. Causes of hepatomegally 6 items.

All that you need in hepatology is just to remember & enumerate these items ($6 \times 16 = 96$ items) , Try to recall these 96 items every night.



Liver function tests

I – Plasma proteins:

- Total proteins : 6 – 8 gm %
- Albumin : 4 – 5 gm % (Totally formed in the liver)
- Globulins : 2 – 3 gm % (α , B in the liver, δ in RES)
- Albumin : globulin (A : G ratio) = 2 : 1

- The liver is the principle site of synthesis of all circulating proteins EXCEPT δ globulins (immunoglobulins), which are produced in the reticuloendothelial system (RES)
- It synthesizes all coagulation factors EXCEPT factor VIII.
- Amino acids are degraded by transamination & oxidative deamination to produce ammonia, which is then converted to urea by the liver and excreted by the kidneys.

In chronic liver disease:

- $\downarrow$ Albumin, $\uparrow$ globulins (to maintain normal total plasma proteins)
- $\downarrow$ A/G ratio & may be **reversed**.
- Albumin is NOT affected in acute liver diseases.

δ globulins increase in liver diseases due to stimulation of antibody against :

- Antigen released from damaged liver cells.
- Antigens absorbed from gut & not cleared by the diseased liver.
- Viral antigen.

Ask for immuno-electrophoresis to know the type of Ig MCQ

- IgG : chronic active hepatitis.
- IgA : Alcoholic liver disease.
- IgM : 1ry biliary cirrhosis.

II – Fat metabolism : (Cholesterol : 150 – 250 mg %)

- Normally cholesterol is esterified in liver & excreted in bile, So :
- **In obstructive jaundice:** ↑↑ cholesterol with normal esterification.
- **In liver cell failure:** normal level of cholesterol with ↓↓ esterification.

N.B. Hepatocytes have a great power for excretion of cholesterol so, it is normal even in LCF.

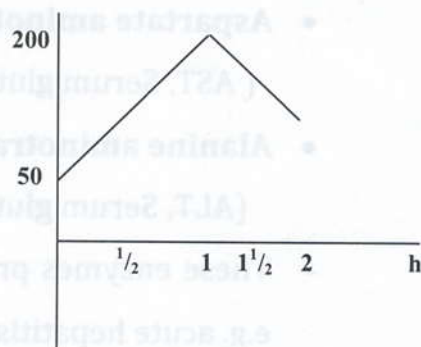
III- Carbohydrate metabolism :

Role of liver in CHO metabolism: (Carbohydrate buffer)

- During fasting : ↑ glucogenolysis & gluconeogenesis → ↑ glucose level.
- After feeding : ↑ glucogenesis → ↓↓ glucose level.
- In prolonged starvation : ketone bodies & fatty acids are used as alternative sources of fuel and the body tissues adapt to a lower glucose requirement.

Blood sugar curve : Lag sugar curve

- During fasting : hypoglycemia.
- After feeding : ↑ glucose level
(> 180 mg % so may appear in urine)



DD of lag sugar curve:

- Chronic liver disease.
- Hyperthyroidism.
- After gastrectomy.

IV- Bilirubin : see jaundice

- **Total serum bilirubin :** (N : 1 mg %) : It ↑ in all types of jaundice.
- **Unconjugated bilirubin:**
 - Normally > 80% of total bilirubin. (0.8 mg%)
 - ↑ in hemolytic jaundice & hepatocellular jaundice.
- **Conjugated bilirubin:**
 - Normally < 20% of total bilirubin. (0.2 mg%)
 - ↑ in obstructive jaundice & hepatocellular jaundice.

- **Bilirubin in urine:**
 - Normally there is no bilirubin in urine.
 - Bilirubin is present in urine in obstructive & hepatocellular jaundice.
- **Urobilinogen in urine:** (colorless)
 - ↑ in hemolytic & hepatocellular jaundice.
 - ↓ in obstructive jaundice.
- **Stercobilinogen in stool:**
 - ↑ in hemolytic jaundice.
 - ↓ in obstructive & hepatocellular jaundice.
- **Bile salts** : Appear in urine in obstructive jaundice → frothy urine.

V- Enzymes :

1- Transaminases :

- **Aspartate aminotransferase :**
(AST, Serum glutamic oxalocetic transaminase, SGOT) : 8 – 40 u/l
- **Alanine aminotransferase**
(ALT, Serum glutamic pyruvic transaminase, SGPT) : 5-30 u/l
- These enzymes present within hepatocytes & released in liver diseases
e.g. acute hepatitis : ↑ (up to 20 fold) -chronic active hepatitis : ↑ (3-5 fold)
- **SGPT** is more **sPecific** for liver diseases than SGOT.
- SGOT may increase also in myocardial infarction & muscle injury.

2- Alkaline phosphatase (ALP) : 3-13 king Armstrong units or 40 – 180 u/l.

- This is present in liver, bone, intestine & placenta.
- Moderate ↑↑ (13 – 30 KAU) : in hepatic failure.
- Marked ↑↑ (> 30 KAU) :
Obstructive Jaundice, Space occupying lesions, bone disease.

3- δ glutamyl transpeptidase (δGT) & 5-nucleotidase:

- To decide that the high level of ALP is due to liver disease & not bone disease.
- If the ALP is normal, a raised serum δGT is a good guide to alcohol intake.

VI- Prothrombin time (PT): Normally 12 : 14 seconds.

- It is prolonged in:

- Acute & chronic liver cell failure : it's due to short half life of Coagulation factors.
- Obstructive Jaundice : due to vitamin K deficiency.

- Importance of PT:

- ➔ To assess the severity & prognosis of liver diseases.
- ➔ Follow up in patient under anticoagulant.
- ➔ Before any invasive technique e.g. liver biopsy.

VII - Alpha fetoprotein: Normally it is < 20 ng / ml.

- Marked elevation (> 2000 ng / ml): highly suggestive for hepatoma.
- Mild or moderate elevation:
 - Cirrhosis.
 - Hepatitis.
 - Pancreatitis.
 - GIT tumor.
- Normal levels of α fetoprotein do not exclude hepatoma.

VIII- Bromosulphalein test (BSP):

For detoxifying function of the liver not performed now because of its side effects.

Immunological tests :

- ✓ Antimitochondrial antibody (AMA) : 1ry biliary cirrhosis (95%)
- ✓ Anti- nuclear & anti-smooth muscle antibodies : autoimmune hepatitis.
- ✓ Antinuclear cytoplasmic antibodies : primary sclerosing cholangitis.



LIVER CIRRHOSIS

Definition :

Cirrhosis is defined as **fibrosis & nodular regeneration** resulting from **hepatic injury**, ending in **loss of normal liver architecture**.

Pathogenesis:

- i- The main damage in cirrhosis is triggered by scarring (fibrosis) that occurs from repeated injuries due to alcohol, viruses,.....
- ii- In response to the scarring, liver cells regenerate in abnormal pattern & form nodules around the scar → irreversible loss of architecture.
- iii- The scar tissue & regenerated nodules block the flow of blood and bile through the liver, preventing it from working as it should.

Etiology:

- 1- **A**lcoholic cirrhosis (Laennec's cirrhosis).
- 2- **B**iliary cirrhosis.
- 3- **B**ilharziasis ?
- 4- **C**hronic hepatitis (**Post hepatitis cirrhosis**).
- 5- **C**ardiac cirrhosis.
- 6- **C**ryptogenic (Idiopathic) cirrhosis.
- 7- **D**rugs : Methotrexate , INH , Methyldopa , Amiodarone.
- 8- **M**etabolic :
 - Hemochromatosis. (↑ Fe)
 - Hepatolenticular degeneration. (↑ Cu)
- 9- **M**iscellaneous :
 - Severe malnutrition.
 - α₁ antitrypsin deficiency.

Classification of cirrhosis:

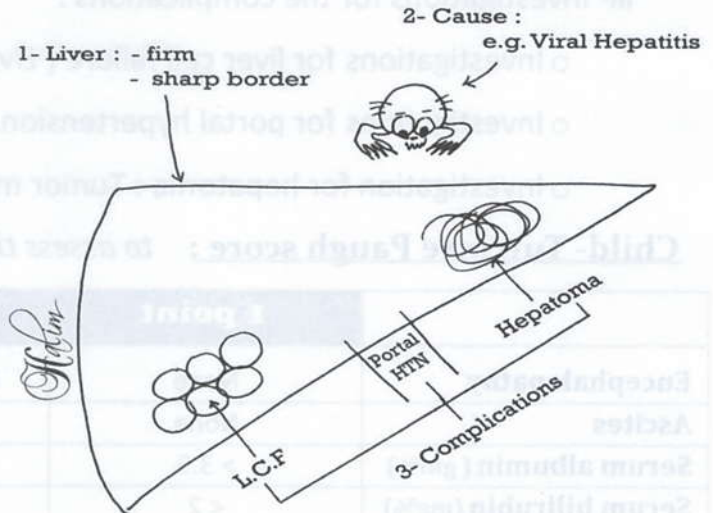
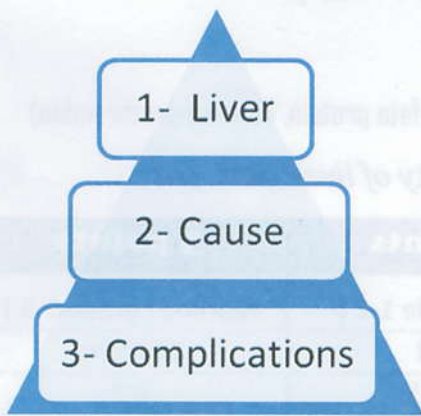
- i. Etiological classification.
- ii. Morphological classification: Micronodular , Macronodular , Mixed.
- iii. Functional classification : Compensated & decompensated cirrhosis.
- iv. Child's classification : to assess the severity of liver cirrhosis.

Clinical picture:

a- Compensated cirrhosis (*Asymptomatic*) : No LCF or portal hypertension

Many patients with liver cirrhosis are asymptomatic for years.

b- Decompensated cirrhosis (*Manifest cirrhosis*) :



i. **Liver :**

- Firm & Sharp border .
- Shrunken. (*the liver may be enlarged in early cases but with progression of the disease ,it shrinks*)

ii. **Clinical picture of the cause** e.g.

- Post hepatitis: history of hepatitis ...
- Alcoholic cirrhosis : history of chronic alcohol intake.
- Hemochromatosis: Bronzed DM....

iii. **Clinical picture of the complications :**

- Liver cell failure : see later.
- Portal hypertension : see later
- Hepatoma may occur : see later

Investigation:

- i- Investigations for the cause e.g. for hepatitis.
- ii- Investigations for the liver :
 - Liver imaging : ultrasound , CT.
 - Liver biopsy is the surest diagnosis.
- iii- Investigations for the complications :
 - Investigations for liver cell failure (*Liver function tests*).
 - Investigations for portal hypertension.
 - Investigation for hepatoma : Tumor marker (α -feto protein, carboxy prothrombin)

Child- Turcotte Paugh score : to assess the severity of liver cirrhosis

	1 point	2 points	3 points
Encephalopathy	None	Mild (grade 1-2)	Marked (grade 3-4)
Ascites	None	Mild	Marked
Serum albumin (gm%)	> 3.5	3 - 3.5	< 3
Serum bilirubin (mg%)	< 2	2 - 3	> 3
INR (International normalized tissue)	< 1.7	1.7 - 2.3	> 2.3

A patient is considered to be :

- ➡ Child class A : < 7 points
- ➡ Child class B : 7-9 points
- ➡ Child class C : > 10 points.

Treatment:

Liver damage from cirrhosis can't be reversed, but treatment can stop or delay further progression and reduce complications.

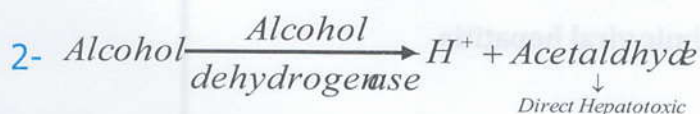
- i- Treatment of the cause e.g. interferon for viral hepatitis.
- ii- Treatment of liver cell failure.
- iii- Treatment of portal hypertension.
- iv- Drugs to decrease liver fibrosis (*Antifibrotic*) : still under trial
 - Colchicine → ↑ collagen destruction.
 - Penicillamine → ↓ collagen synthesis.
- v- **Hepatic transplantation** is the best hope but many patients are not suitable.

Alcoholic Cirrhosis

Etiology:

Alcoholic cirrhosis usually develops after more than 10 years of heavy drinking

1- Alcohol $\rightarrow$ $\downarrow$ appetite & malabsorption $\rightarrow$ nutritional cirrhosis.



Pathology:

- **M**icronodular cirrhosis.
- **M**allory bodies: eosinophilic deposits.

Clinical picture:

- 1- General C/P of cirrhosis. (LCF > pH)
- 2- C/P of the cause : History of prolonged alcohol intake > 10 years (*Alcoholism*)

Features of chronic alcoholism:

- GIT : Gastritis, hepatitis, pancreatitis, malabsorption.
- CNS: Tremors , Amnesia (*Korsakow's syndrome*), headache & migraine.
- Cardiac : cardiomyopathy.
- Blood: hemolytic anemia.
- Immune: recurrent infection.
- Metabolic: Hypoglycemia, hyperlipidemia.
- Bilateral parotid enlargement.

Investigation:

general investigations for cirrhosis.

Treatment:

- Stop alcohol intake.
- General measures for cirrhosis.
- Essential amino acids.
- Colchicine , Cortisone.

N.B. Alcoholic liver diseases:**1- Fatty liver (reversible) :**

Alcohol → ↑ fat entry to hepatocytes.

→ ↓ fat secretion from hepatocytes.

2- Alcoholic hepatitis : mimic viral hepatitis

- ↑↑ IgA
- If ratio of SGOT: SGPT > 2:1 → suggests alcohol hepatitis.

3- Cirrhosis (LCF > PH)**Post hepatitis Cirrhosis**

Etiology: following virus B , C & D.

Pathology:

- Pathology of cirrhosis itself.
- Ground glass appearance.
- +ve orcién stain
- Features of chronic active hepatitis.

Clinical picture:

- Clinical picture of cirrhosis.
- Past history of virus hepatitis. (see later)

Investigation:

- Investigation for cirrhosis.
- Detection of hepatitis markers.

Treatment:

- General measures for cirrhosis.
- Treatment of chronic active hepatitis.
- Hepatitis B vaccine for prevention.

Bilharziasis

(pH > LCF) details : see later

- Bilharziasis causes portal hypertension & periportal fibrosis but not cirrhosis.

Indeed, liver function remains remarkably good in chronic infection.

- Cirrhosis with marked fibrosis may occur by 2 mechanisms :

1- Combined etiology with virus C.

2- Ag- Ab complex.

Cardiac Cirrhosis

Etiology: *Due to long standing liver congestion* (Rare & Late)

- 1- RSHF
- 2- Tricuspid valve disease.
- 3- Constrictive pericarditis & pericardial effusion
- 4- Inferior vena cava obstruction.
- 5- Budd - Chiari syndrome (obstruction of the large hepatic veins)
- 6- Veno-occlusive disease. (obstruction of the small intrahepatic veins).

Clinical picture: Again: cardiac cirrhosis is rare & late.

- General features of cirrhosis. (Portal hypertension occurs before liver cell failure)
- Liver is enlarged, tender , soft then firm with sharp border.

Investigation:

- The same as cirrhosis.
- Investigation for the cause e.g. echocardiography.

Treatment:

- General measures for cirrhosis.
- Treatment of the causes e.g. heart failure.

Budd–Chiari syndrome

Definition :

It's obstruction of large hepatic veins due to :

- Thrombosis e.g. Polycythemia rubra vera, OCP, PNH, Behcet syndrome, Atrial myxoma, Antiphospholipid syndrome.
- Obstruction (*tumor*).
- Idiopathic.

All of the following may be etiology of Budd–Chiari syndrome EXCEPT :

- a) Congenital hepatic fibrosis.
- b) Antiphospholipid syndrome.
- c) Oral contraceptive pills.
- d) Right atrial myxoma.

C / P :

- Acute stage :
 - Triad of : Abdominal Pain, Ascites , **Rapidly enlarged** tender liver.
 - Manifestations of fulminant hepatic failure may occur.
- Chronic stage: features of cardiac cirrhosis.

Edema LL & dilated veins over the abdominal wall & back suggest IVC obstruction.

Investigations :

1) Laboratory :

- Elevated liver enzymes & bilirubin.
- Assessment of hypercoagulability state.

2) Imaging :

- Duplex ultrasound.
- CT & MRI of the abdomen.
- Hepatic venography : diagnostic but invasive.

3) Liver biopsy.

Treatment :

- ➡ Long term anticoagulant in a chronic cases.
- ➡ Thrombolytic therapy in acute cases.
- ➡ Surgical shunt or TIPS (Transjugular Intrahepatic Portosystemic Shunt) : to divert blood flow around the obstruction.
- ➡ Needless to say plus : general treatment of cirrhosis e.g.
 - Control of ascites & hepatocellular failure.
 - Liver transplant : is an effective treatment for Budd–Chiari. It is generally reserved for patients with fulminant hepatic failure.

Biliary Cirrhosis

- It's cirrhosis caused by prolonged biliary obstruction.
- Bile is very irritant to the hepatocytes if retained.

(A) Primary biliary cholangitis : (Primary biliary cirrhosis)

- Primary biliary cholangitis is the new name for primary biliary cirrhosis
- Autoimmune disease leading to destruction of intra-hepatic bile duct.

Clinical picture : ♀ 30-50 Y (It is 10 times commoner in women than men)

- Asymptomatic ($\frac{1}{3}$)
- Fatigue (most common).
- Itching occurs months before jaundice because retention of bile salts can occur before significant retention of bilirubin. (the cause of itching is still questionable)
- Obstructive Jaundice.
- Clubbing.
- Hepatomegaly.
- Malabsorption of fat - soluble vitamins (A , D , E , K) :
 - Vit D → Osteomalacia.
 - Vit K → Bleeding tendency.
- Associated immune disorders : SLE, 30% of patients have thyroid disorders.
- Xanthelasma 2ry to hypercholesterolemia.
- Complications of cirrhosis e.g. LCF, Portal hypertension.

The disease is more aggressive in younger patients

Medical causes of itching:

- | | |
|--------------------------|---------------------|
| • 1ry biliary cirrhosis. | • Hemolytic anemia. |
| • Obstructive Jaundice. | • Polycythemia. |
| • DM | • Lymphoma. |
| • CRF | • Leukemia. |



Investigation:

- i. Serology : It's an autoimmune disorder so, there are : **MCQ**
 - **Anti-mitochondrial antibody (AMA)** : +ve in 95% . Notice that AMA is an important diagnostic feature but titre is not predictive of outcome.
 - ↑ Ig**M**.
- ii. Liver function test : **MCQ**
 - The most characteristic blood test is elevation of **Alkaline phosphatase**.
 - **PT**, bilirubin and albumin tend to be **normal** until late in the disease.
- iii. Liver imaging : US , CT → enlarged liver with no dilated intra-hepatic biliary radicals.
- iv. Liver biopsy is diagnostic.

Treatment:

- Ursodeoxycholic acid (UDCA) is first line therapy & should be used in all patients regardless of symptoms status.
- Immunosuppressive: Pencillamine, Azathioprine.
- Symptomatic treatment : e.g. Cholestyramine for itching.
- **Liver transplantation is the most curative treatment.**
- **Cortisone is contraindicated** as it increases osteomalacia and osteoporosis.

B) Secondary biliary Cirrhosis:

- i. **Extrahepatic** : stone, stricture.

N.B. Cancer head of pancreas usually of short duration so cirrhosis usually doesn't occur.

- ii. **Intrahepatic**: See obstructive Jaundice.

- **Clinical picture, investigations & treatment** : of obstructive jaundice. *see later*

How to differentiate between extrahepatic & intrahepatic biliary obstruction?

1- US :

- Intrahepatic → constriction of intrahepatic bile radicals.
- Extrahepatic biliary obstruction → dilation of intrahepatic bile radicals.

2- Cortisone test.

3- Clinical differentiation : " see jaundice "



Hemochromatosis "*bronzed diabetes*"

Definition: (autosomal recessive disorder) The responsible gene is : HFE gene on chromosome 6

It's a hereditary disease characterized by excessive absorption of iron resulting in ↑ of total body iron with its deposition in several organs.

Etiology:

- Excessive iron absorption due to absence of mucosal block (autosomal recessive)
- Here, body iron reaches up to 60 gm (N : 3-4 gm)

Clinical Picture: *More common in ♂ (no menstruation)*

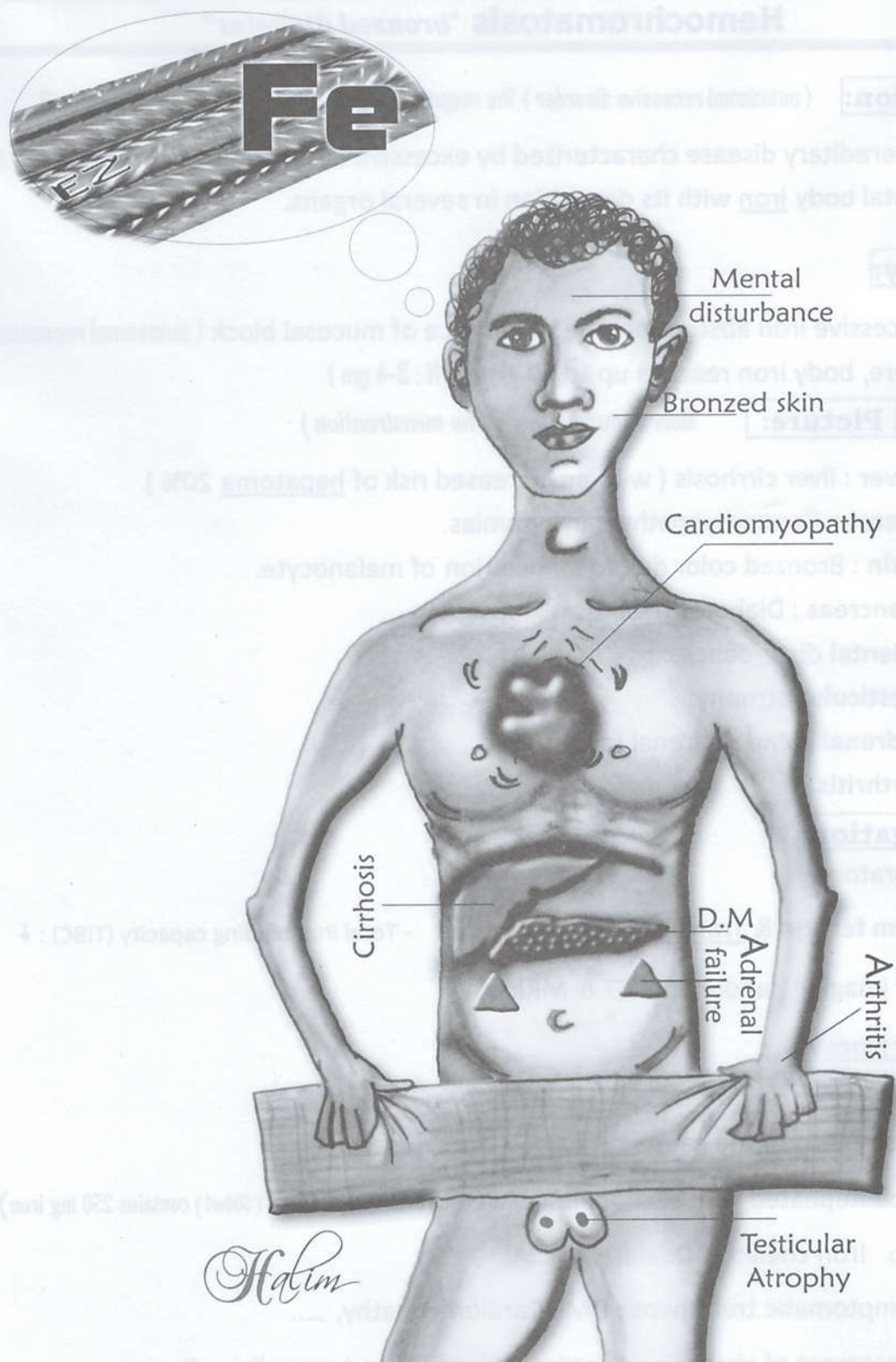
- 1- **Liver** : liver cirrhosis (with an increased risk of hepatoma 20%)
- 2- **Heart** : Cardiomyopathy , arrhythmias.
- 3- **Skin** : Bronzed color due to stimulation of melanocyte.
- 4- **Pancreas** : Diabetes mellitus.
- 5- **Mental** disturbance.
- 6- **Testicular** atrophy.
- 7- **Adrenal gland** : adrenal failure.
- 8- **Arthritis**.

Investigation:

- i. **Laboratory** :
 - Serum ferritin & Transferrin saturation : ↑ - Total iron binding capacity (TIBC) : ↓
- ii. **Liver imaging** : abdominal CT & MRI.
- iii. **Liver biopsy**.

Treatment:

- i. Treatment of the cause :
 - Repeated venesection: once/week (every bag of blood (500ml) contains 250 mg iron)
 - Iron chelator: Desferal
- ii. Symptomatic treatment : DM , Cardiomyopathy,
- iii. Treatment of cirrhosis : liver transplant for end stage liver disease.



Hemochromatosis

Hepatolenticular Degeneration "Wilson's disease"

Etiology: (autosomal recessive disorder) The responsible defective gene is : ATP 7B on **chromosome 13**.

In Wilson's disease copper absorption is normal but there is a deficiency in hepatic formation of "Ceruloplasmin" which is the principal transport protein for copper & necessary for biliary excretion → so free copper will be released to the blood → Abnormal deposition of Cu in several organs (liver , brain , eye) & urinary excretion of copper is increased.

Clinical picture:

- **Liver** : hepatitis (self limited) , may progress to cirrhosis.
- **Lentiform nucleus** (Basal ganglia) → extrapyramidal manifestation e.g. tremors.
- **Kidney** → renal tubule damage which lead to albuminuria & aminoaciduria.
- **Eye** → Kayser – Fleischer ring (green brown ring around the edge of the iris)

Investigation:

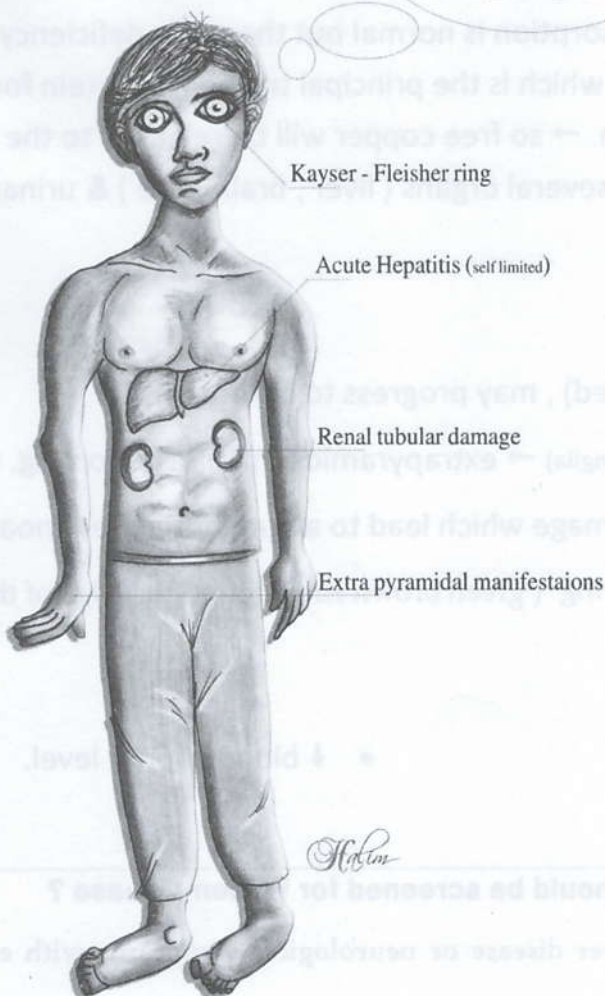
- ↓ ceruloplasmin level.
- ↓ blood copper level.
- Liver biopsy.

- **The question now is : who should be screened for Wilson disease ?**
- Anyone with unexplained liver disease or neurological symptoms with evidence of liver disease.

Treatment:

- Treatment of the cause :**
 - Penicillamine or trientine hydrochloride : increase urinary excretion of Cu
 - Zinc acetate : blocks the absorption of copper.
 - Restriction of copper in diet : ↓ liver , mushrooms.
- symptomatic treatment.**
- Treatment of cirrhosis : liver transplant.**

Cu

*Wilson's disease*

Notes

Etiology :

- 1. Infection: viral hepatitis, B, C, D
- 2. Chemicals :

o Alcohol

o DDT, Malathion, Parathion, etc.

- 3. Physical: Severe burns & hyperthermia

4. Terminal stage of :

o Liver cirrhosis

o obstructive jaundice

o chronic hepatitis

o pregnancy

Clinical Picture of liver cell failure:

- 1. Fatigue, anorexia, loss of weight

- 2. Fever

- 3. Tender hepatomegaly

- 4. Jaundice

- 5. Ascites

- 6. Esophagopathy

- 7. Skin manifestations

- 8. Endocrine manifestations (hypogonadal)

- 9. Cardiovascular manifestations

- 10. Hematological manifestations

- 11. Hepatorenal syndrome

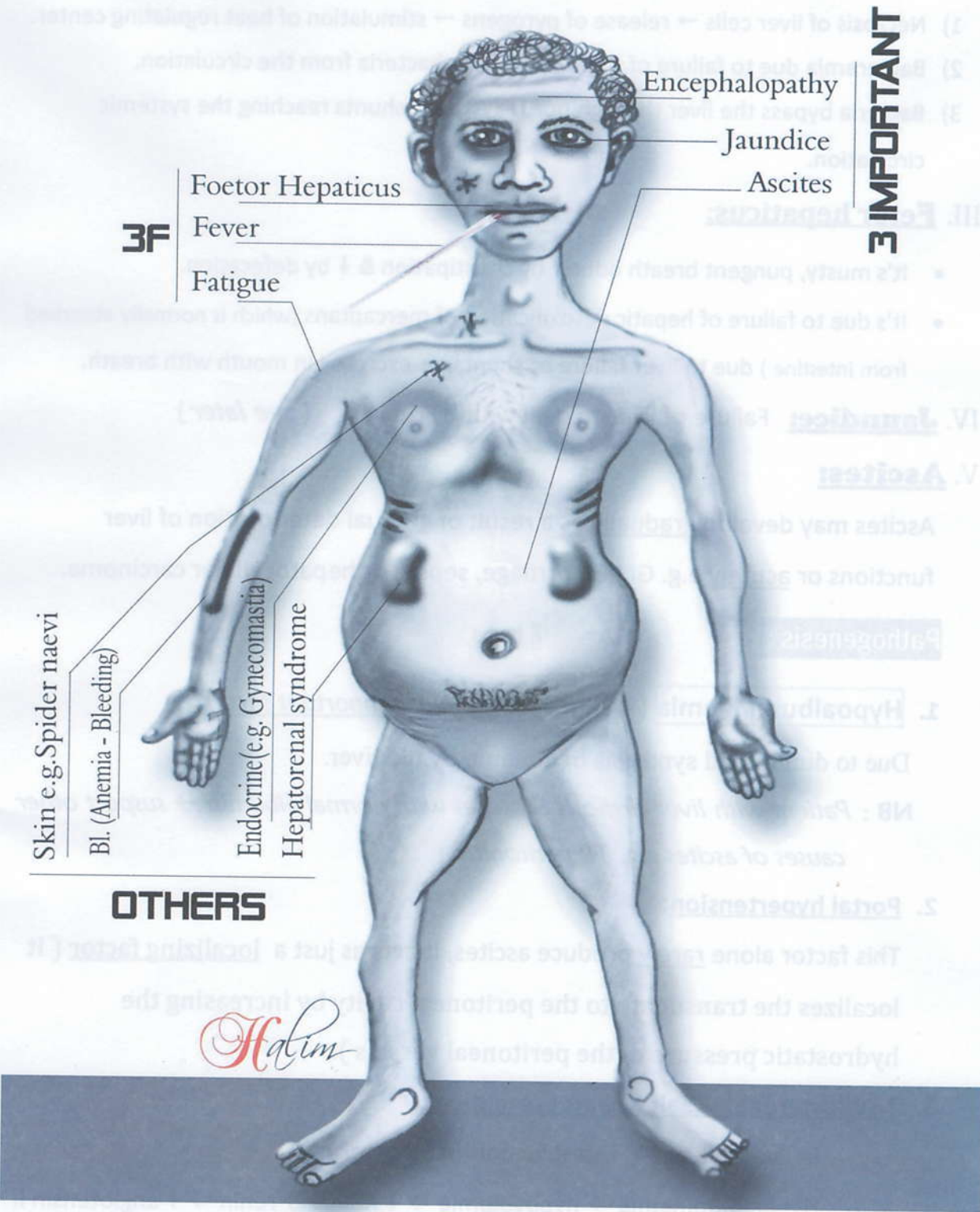
LIVER CELL FAILURE

Etiology :

1. Infections: viral hepatitis. B, C, D
2. Chemicals :
 - Alcohol .
 - DDT, Halothan, Paracetamol , INH
3. Physical: Severe burns & hyperthermia.
4. Terminal stage of :
 - Liver cirrhosis.
 - obstructive jaundice
 - chronic hepatitis.
 - malignancy

Clinical Picture of liver cell failure:

1. Fatigue, anorexia, loss of weight
2. Fever.
3. Feter hepaticus.
4. Jaundice
5. Ascites
6. Encephalopathy
7. Skin manifestations.
8. Endocrinal manifestations. (Hormonal)
9. Cardiovascular manifestations.
10. Hematological manifestations.
11. Hepatorenal syndrome.



I. Fatigue, anorexia & loss of weight.**II. Fever:** (low grade & prolonged) due to :

- 1) Necrosis of liver cells → release of pyrogens → stimulation of heat regulating center.
- 2) Bacteremia due to failure of the liver to clear bacteria from the circulation.
- 3) Bacteria bypass the liver through porto-systemic shunts reaching the systemic circulation.

III. Feter hepaticus:

- It's musty, pungent breath odor ↑ by constipation & ↓ by defecation.
- It's due to failure of hepatic detoxification of mercaptans (which is normally absorbed from intestine) due to liver failure or shunts. → excreted in mouth with breath.

IV. Jaundice: Failure of liver to deal with bilirubin (see later)**V. Ascites:**

Ascites may develop gradually as a result of gradual deterioration of liver functions or acutely e.g. GI hemorrhage, sepsis, or hepatocellular carcinoma.

Pathogenesis :**6 Items****1. Hypoalbuminaemia** (< 3gm%) : The most important factor.

Due to diminished synthesis of albumin by the liver.

NB : Patient with liver cirrhosis & ascites with normal albumin → suspect other causes of ascites e.g. TB peritonitis.

2. Portal hypertension:

This factor alone rarely produce ascites, it acts as just a localizing factor (It localizes the transudate to the peritoneal cavity by increasing the hydrostatic pressure of the peritoneal vessels).

3. ↑ Aldosterone ⇒ Salt & water retention :

- In liver failure ⇒ ↓ destruction of aldosterone.
- Hypoalbuminemia ⇒ hypovolemia ⇒ ↓ RBF ⇒ ↑ renin ⇒ ↑ angiotensin II ⇒ ↑ aldosterone.

4. Peripheral arterial & splanchnic vasodilatation theory :

This is mediated by accumulation of vasodilators (mainly nitric oxide) $\Rightarrow$ pooling of blood into peripheral & splanchnic arteries $\Rightarrow$ vascular underfilling is sensed by the kidney $\Rightarrow$ This leads to activation of the **renin-angiotensin system** $\Rightarrow$ Salt retention $\Rightarrow$ Ascites.

5. Lymphorrhea: (liver weeping) 💧💧

Post sinusoidal obstruction $\rightarrow$ $\uparrow$ lymph production into peritoneum.

6. Associated factors: SBP, malignancy, T.B. peritonitis....

Spontaneous bacterial peritonitis: (SBP)

- Infection of the peritoneal cavity in absence of known etiology.
- Occurs in 10% of cirrhotic patients.
- Due to loss of detoxification function of the liver.
- The prognosis is very bad.
- c/p :
 - i deterioration of liver function, e.g. $\uparrow$ encephalopathy, ascites or jaundice.
 - ii- resistance to diuretics may be a sign of SBP.
 - iii- High fever, sever abdominal pain, tenderness.

NB : Cirrhotic patients with ascites and evidence of any clinical deterioration should undergo diagnostic paracentesis to exclude SBP.

○ **Diagnosis** :

The key of diagnosis is examination of the ascetic fluid.

- **Neutrophils count** > 250 cells / mm^3 .
- Culture: monomicrobial e.g. E.coli.

○ **Treatment** :

Cefotaxime: 2 gm t.d.s...IV or Ciprofloxacin 400 mg/12h for 5 - 10 days.

Clinical picture & Investigations of a case of ascites:see later**Treatment :****6 Item**

- 1- Salt restriction. < 2 g /d. cornerstone of therapy.
- 2- Diuretics :
 - i. Spirinolactone in full dose 100-400mg/ d... drug of choice.
 - ii. Lasix (40-160 mg/d)

The maximum amount of fluid transported from peritoneum to the blood is 500-700 cc/d, so any more lasix → general dehydration of the body without improvement of ascites. (ascites without edema LL)

3- Tapping (paracentesis) : indicated in the following conditions :

- Sampling.
- To relieve respiratory distress.
- To relieve compression on the kidney.

4- Albumin (infusion) : to correct the osmotic pressure of the plasma.**5- Peritoneo-venous shunt : Le Veen shunt.**

- To drain the ascetic fluid into the circulation.
- Complications : Septicemia , DIC , Hypervolemia & Heart failure.

6- Treatment of the cause : Antibiotics for SBP , liver transplantation.

✓ Ascites must not be treated if there are marked manifestations of liver cell failure e.g. hepatic encephalopathy.

✓ **W**et & **W**ise better than **D**ry & **D**rowsy. ☺

Refractory ascites :*Details : see later*

Ascites with lack of response to : 400 mg spironolactone plus 160 mg lasix daily with salt restricted diet for at least one week.

VI. Skin manifestations: Due to accumulation of vasodilator material (VDM) e.g. estrogen, Nitric oxide.

1. Palmar erythema:

- Erythema in head of metacarpal bones, thinner & hypothermic with central pallor.
- Also seen in pregnancy, thyrotoxicosis or RA.



2. Spider naevi:

- Vascular lesions usually found in the distribution of SVC (on the face, trunk & upper part of the arms).
- They consist of a central dilated arteriole with radiating capillaries.
- Compression of the central arteriole causes blanching of the radiating capillaries.
- They are also found in pregnancy.



3. Paper money skin:

Numerous small vessels scattered in skin over bony areas, dorsum of foot & hand, forehead, chest.

4. White nail: white zone at the tip of the nail.

VII. Endocrinal manifestations: may be due to disturbance of sex hormones

- ♂ — { Gynecomastia.
Female distribution of suprapubic hair.
Impotence, ↓ libido & testicular atrophy.

- ♀ — { Amenorrhea & sterility.
Atrophy of breast & ↓ libido.

- ↑ Aldosterone & ADH (in males & females)

VIII. Cardiovascular manifestations: (VDM)

i- **Hyperdynamic circulation:** due to :

- Anemia.
- Toxic product are vasodilators (VDM)

ii- **Cyanosis & clubbing** : due to

- Opening of intrapulmonary A.V. shunt. → d. to (VDM)
- Porto-pulmonary shunts.
- Basal lung collapse due to ascites.

iii. **Cardiac dysfunction** : due to

- Neurohumoral hyperactivity (RAAS) leading to myocardium growth and fibrosis with disturbed relaxation.
- An inhibitory effect of circulating cytokines (e.g. nitric oxide) on ventricular function.

This cardiac dysfunction remains clinically silent masked by the afterload reduction that is observed in cirrhosis. So, cardiac reserve may be diminished and acute heart failure may manifest after TIPS or liver transplantation.

IX. Hematological manifestations:

i- **Anemia:**

➤ **Normocytic normochromic** :

- BM depression by toxins.
- Hyposplenism.

➤ **Microcytic hypochromic:** Iron deficiency anemia due to chronic Blood loss.

➤ **Macrocytic** : Vit B₁₂ & folic acid deficiency.

ii- **Bleeding tendency: due to**

- Hypoprothrombinemia.
- Hypofibrinogenemia.
- ↓ factors II, VII, IX, X (1972)
- ↓ vit. K
- Hypersplenism → thrombocytopenia.

X. Hepato-renal Syndrome: (HRS)

- Functional renal failure with normal renal histology in patients with advanced liver cirrhosis or fulminant hepatic failure.

- **Pathophysiology :**

The hallmark of HRS is renal vasoconstriction. The exact mechanism is unknown, but may be due to :

1) Peripheral splanchnic arterial vasodilation theory : (*Underfill theory*)

Splanchnic vasodilatation due to portal hypertension & accumulation of VDM e.g. nitric oxide $\Rightarrow$ pooling of blood into peripheral & splanchnic arteries $\Rightarrow$ vascular underfilling is sensed by the kidney $\Rightarrow$ This leads to activation of the **renin-angiotensin system** $\Rightarrow$ renal vasoconstriction.

2) Hypovolemia due to hypoalbuminemia, ascites, diuretics.

3) Cardiac dysfunction associated with hepatic disease is a recent theory.

- **Criteria of diagnosis :**

1. Chronic or acute liver disease with advanced hepatic failure & portal hypertension.
2. Low glomerular filtration rate (serum creatinine >1.5 mg% or 24-hr creatinine clearance <40 mL/min).
3. Absence of shock or current treatment with nephrotoxic drugs.
4. No sustained improvement after withdrawal of diuretics & expansion of plasma volume.
5. No ultrasonographic evidence of obstructive uropathy or parenchymal renal disease.



- **Types :**

- Type 1 HRS : Rapidly progressive type with high mortality rate. There is a doubling of serum creatinine to a level greater than 2.5 mg/dL in <2 weeks.
- Type 2 HRS : Slower progressive course with a serum creatinine of >1.5 mg/dl with better prognosis.

- **Precipitating factors :**

1. Large volume paracentesis of ascites without volume expansion.
2. Systemic infections e.g. SBP.
3. Excessive diuretic therapy.
4. Diminished intravascular volume e.g. diarrhea.

- **Prognosis :** is very bad.

- **Treatment :**

- IV albumin (plasma expansion)
- Systemic vasoconstrictors e.g. somatostatin analogs (octreotide).
- Liver transplantation is the best choice.



XI. **Hepatic Encephalopathy:**

Definition :

It's a neuropsychiatric syndrome that is seen in patients with acute or chronic liver cell failure or porto-systemic shunting.

Pathogenesis :

1- Production of toxic substances : by the action of bacteria on intestinal proteins

- Ammonia : It interferes with creb's cycle : (glutamic acid $\xrightarrow{\text{NH}_3}$ glutamine $\rightarrow \downarrow$ CNS)
- Others : inhibitory neurotransmitters
e.g. γ aminobutyric acid (GABA), Mercaptan, benzodiazepine like compounds.

2- Disturbance of amino acids :

Decreased branched-chain & increased aromatic amino acids leading to :

- Decreased production of normal neurotransmitters (as noradrenaline)
- Formation of false neurotransmitters (e.g. octopamine).

3- Alkalosis & hypokalemia :

- $\downarrow$ glucose entry to cerebral cells $\rightarrow$ coma.
- $\uparrow$ the renal production of ammonia.
- $\uparrow$ the permeability of BBB to some of toxic substances.

Precipitating factors :

1- **GIT bleeding.**

2- $\uparrow\uparrow$ protein intake.

3- Old Blood transfusion.

4- Aspiration of ascites.

5- Diuretics : Frusemide (*lasix*)

6- Others :

- Drugs : Morphine , Benzodiazepines.
- SBP (*spontaneous bacterial peritonitis*).
- Surgery e.g. porto-systemic shunts.

6 Items

$\uparrow$ ammonia

$\downarrow$ K⁺ & alkalosis

Clinical picture:

Pre coma: 2 S A D

Coma

i- Pre Coma:**6 Items**

- **S**leep: Inverted sleep rhythm (day/night reversal), any metabolic error can do that.
- **S**peech: slow, slurred or monotonous.
- **A**pathy: slow response to questions.
- **A**sterixis: (Flapping tremors).
- **D**isorientation: for time, place, persons.
- **D**isturbed behavior : childish attitude , phasic excitation & depression.

ii- Coma: Irritable coma.

DD of irritable coma :

Hypoglycemic coma, Hepatic coma.

Causes of bilateral asterixis :

- Any organ failure : hepatic, renal, cardiac or respiratory failure.
- Metabolic abnormalities : hypoglycemia, hypokalemia and hypomagnesemia.
- Drugs : alcoholism, phenytoin, barbiturate.
- Wilson's disease.

Unilateral asterixis : focal brain lesion
e.g. midbrain, internal capsule.

Clinical stages of hepatic encephalopathy : (*for postgraduates*)

Stage	Mental status	Asterixis	EEG
I	Mild confusion , slow mentation , inverted sleep rhythm.	+/-	Triphasic waves (5 cycles/sec)
II	- Lethargy. - moderate confusion & disorientation	+	Triphasic waves
III	- Marked confusion & disorientation - Sleepy but responds to pain & voice	+	Triphasic waves
IV	Coma (unrousable, unresponsive to voice & pain).	- (Decerebration)	Delta activity (2 cps)

Diagnosis : The diagnosis can usually be made clinically, but when doubt exists :

- Electroencephalogram (EEG) : shows diffuse slow triphasic waves.
- Ammonia level : $\uparrow$, It is not a sensitive or specific test for hepatic encephalopathy.

Treatment of hepatic encephalopathy: 6 Items

1- Hospitalization in ICU, endoscope should be done to localize the site of bleeding.

2- Diet:

- protein: restricted.
- Carbohydrate : $\uparrow\uparrow \Rightarrow \downarrow$ protein breakdown as a source of energy.
- Fats in small amount $\rightarrow$ mild diarrhea which is useful to wash intestine.
- K excess : fruit juices.

3- Enema / 4h $\Rightarrow$ wash the colon.

4- Antibiotics : to prevent the action of intestinal bacteria on proteins.

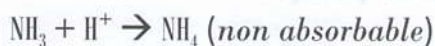
✕ Neomycin 1gm/6h orally. SE : nephrotoxicity or

✕ Metronidazole : 500 mg / 6h . or

✕ Rifaximin : 400 mg t.d.s.

5- Lactulose (30 - 120 ml 3 times daily) : oral or rectal.

- Osmotic diarrhea $\rightarrow$ wash the colon.
- Production of acids . this promotes the conversion of luminal ammonia (NH_3) to ammonium (NH_4)



6- Liver transplantation

Drugs of doubtful value :

- **B**ranchd amino acids.
- **B**romocriptin & L dopa : to improve neurotransmission.
- **B**enzodiazepine antagonists : Flumazenil.
- L-ornithine L-aspartate (Lola) : it reduces the level of ammonia.

Sedatives :

- Should be avoided, but if necessary; give small doses of diazepam.
- Morphine is absolutely contraindicated.

Investigations of LCF:

- Liver function tests :
 - Serum enzymes (AST , ALT) : ↑
 - Serum bilirubin : ↑ (both direct & indirect)
 - Plasma proteins : ↓ albumin , ↑ globulin (reversed A/g ratio).
 - Prothrombin time : prolonged , not corrected by parenteral vitamin K.
- Investigations for the cause :
 - Abdominal US , CT : for cirrhosis.
 - Hepatitis markers : for hepatitis.
- Investigations of ascites.
- Investigations of hepatic encephalopathy.

N.B. Biopsy is very difficult due to bleeding & Ascites.

Treatment of LCF:

- Treatment of the cause : if possible.
- Treatment of ascites: provide that the features of LCF are not sever.
- Treatment of encephalopathy.
- Liver transplantation.

ACUTE (Fulminant) HEPATIC FAILURE**Definition:**

Hepatic failure with **encephalopathy** developing in less than 8 weeks after the onset of jaundice in a patient **without** pre-existing liver disease.

N.B:

- Hyper acute liver failure → within 2 weeks.
- Acute liver failure → within 2-8 weeks.
- Sub acute liver failure → 8 weeks - 6 months.

Etiology:

- **Viral hepatitis.**
- **Paracetamol toxicity** (> 15gm = 30 tab)
 - Its daily dose shouldn't exceed 4g/d, over 15g/d will result in liver injury, >25 → fatal fulminant hepatic failure.
 - Mechanism : An active metabolite of paracetamol is hepatotoxic, It is detoxified by glutathione, & when glutathione stores are depleted, severe liver damage can occur.
 - Antidote : N-acetylcysteine.
- **Alcohol toxicity.**
- **Acute fatty liver of pregnancy :**
 - A rare and serious condition that occurs in the third trimester or the immediate period after delivery. It can be relieved by delivery of the infant.
 - Abnormal fatty acids produced by the fetus pass to the mother & overcome maternal hepatic mitochondrial oxidation system leading to an accumulation in hepatocytes.
 - It is thought to be caused by dysfunction of fatty acid metabolism by mitochondria in the mother, caused by deficiency in the LCHAD (long-chain 3-hydroxyacyl-coenzyme A dehydrogenase) enzyme.
- **Reye's syndrome :**

It is a rare but serious condition, The classic features are a rash, vomiting, and liver damage. It has been associated with aspirin consumption by children with viral infection, so children recovering from flu-like symptoms should never take aspirin.
- **Budd-Chiari syndrome.**

Clinical picture:

- **Encephalopathy** : due to :
 - Severe liver injury leading to $\uparrow$ ammonia.
 - Occurrence of other metabolic complications: Hypoglycemia, hypokalemia, sepsis or brain edema.
- **Coagulopathy** : (bleeding)
- **Jaundice** : is mild in early stages & becomes deep later.
- The condition may be **misdiagnosed** as encephalitis .
- The condition usually ends by **death** due to bleeding, cerebral edema, respiratory & circulatory failure (shock) & other organ failure.

Complications :

- 1) Encephalopathy.
- 2) Cerebral edema : one of the common cause of death in fulminant hepatic failure. It is due to cerebral vasodilatation.
- 3) Respiratory failure : due to pulmonary infections, aspiration in comatosed patients.
- 4) Circulatory failure : hypotension & tachycardia due to vasodilatation.
- 5) Renal failure : sepsis, toxic, hypoxic, or functional. Because of impaired production of urea, blood urea does not represent degree of renal impairment.
- 6) Infection : Bacterial sepsis (80%) & fungal sepsis (30 % of patients).
- 7) Metabolic :
 - Hypoglycemia
 - Hypokalemia.
 - Hyponatremia : due to water retention
 - Hypomagnesemia, Hypocalcemia
 - Acid base disturbance : **Metabolic alkalosis**. Lactic acidosis occurs in paracetamol overdose.

Investigations:**i. Liver function tests :**

- Serum Bilirubin : is elevated. Exceeding 23mg → Poor prognosis.
- Serum enzymes (AST , ALT) : ↑↑ and may remain high or fall later due to extensive loss of liver cells.
- Serum albumin : Normal , but later becomes low if the patient survives for > 3 weeks.
- Prothrombin time : prolonged. (it is used to assess the prognosis)

ii. Investigations for the cause :

- Hepatitis markers.
- Serum drug screen e.g. paracetamol.

iii. Liver imaging : May be small due to hepatic necrosis or may be enlarged due to heart failure, viral hepatitis, or Budd-Chiari syndrome.**iv. CT , MRI of the brain :** to exclude brain lesions.**Prognosis :** (*King's College Hospital criteria*)

Several prognostic scoring systems have been devised to predict mortality and to identify who will require early liver transplant. These include *King's College Hospital criteria*.

i. In a case of paracetamol overdose:

- 1) pH <7.3 or
- 2) All 3 of :
 - INR >6.5 (PT>100 seconds),
 - serum creatinine >3.4 mg/dL
 - Grade 3 or 4 hepatic encephalopathy.

II. Non-paracetamol acute liver cell failure:

- 1) INR >6.5 (PT >100 seconds), or
- 2) Any 3 of the following:
 - Age between 10 and 40 years.
 - Unidentified cause, or Drug toxicity.
 - Duration of jaundice before hepatic encephalopathy >7 days.
 - INR >3.5 (PT >50 seconds)
 - Serum bilirubin >17mg/dL.

Treatment:

- i. Treatment of encephalopathy.
- ii. Treatment of complications.
- iii. Artificial hepatic support : Charcoal filter are used to adsorb toxins from the blood.
- iv. Hepatic transplantation.

PORTAL HYPERTENSION

Definition:

Elevation of portal venous pressure above 12mm Hg (N: 7-10 mm Hg)

Etiology: The most common cause at all is **Liver cirrhosis**

i- Supra hepatic (Cardiac cirrhosis) e.g.

RSHF, TR, Pericarditis, IVC obstruction & Budd Chiari syndrome.

ii- Hepatic (most common) :

➤ **sinusoidal & post sinusoidal :**

○ Liver cirrhosis "the most common cause".

○ Veno-occlusive disease.

➤ **pre sinusoidal :**

○ **S**chistosomiasis (Bilharziasis): peri-portal fibrosis.

○ **C**ongenital fibrosis of portal tract.

○ **H**odgkin's lymphoma, leukemia.

iii- Infra-hepatic : rare

○ Portal vein thrombosis (Hepatoma).

○ Congenital stenosis of portal vein.

○ Extrinsic compression (tumor)

Cirrhosis is the main cause of portal hypertension By:

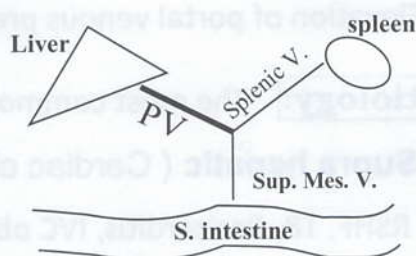
- 1- The trauma that caused cirrhosis creates an arterio-venous fistula between the hepatic arterioles & portal vein.
- 2- Liver fibrosis & regenerative nodules increase the portal pressure by compression.

Pathophysiology:

Portal vein is formed by the union of superior mesenteric & splenic veins.

So, portal hypertension leads to: 

- i. Spleen congestion.
- ii. Intestinal congestion.
- iii. Porto-systemic shunt : in attempt to decompress the portal hypertension.



- ➔ Development of collateral channels : esophageal varices, Caput medusa, Hemorrhoids.
- ➔ Shunting of toxins from the intestine into the general circulation → Hepatic encephalopathy.

Clinical Picture:

6 item

(1) Splenomegaly:

- Dragging pain in the left hypochondrium.
- May be the only clinical evidence of portal hypertension.
- May be associated with hypersplenism, which by turn lead to pancytopenia & bleeding tendency.

No relation between the size of spleen & severity of portal hypertension.

(2) Intestinal congestion:

- **D**istension.
- **D**yspepsia.

(3) Liver: firm & sharp border (cirrhotic liver)

(4) Ascites : SAAG > 1.1

Portal hypertension is a localizing factor rather than a cause.

- (5) Encephalopathy :
- Pre-coma: 2S, 2A , 2D.
 - Irritable come.

(6) Porto-systemic shunt: In attempt to decompress the portal hypertension.

Main sites of the collaterals :

Site	Portal Circulation	Systemic C.	Clinical presentation
1- Lower end of esophagus	Coronary veins of stomach	Azygos vein	Esophageal varices with or without bleeding
2- Around the umbilicus	Umbilical vein in flaciform ligament	Veins of anterior Abdominal wall	Caput medusa (flow away from umbilicus)
3- Anal canal	Superior & middle rectal veins	Inferior rectal vein	May be mistaken for hemorrhoids

N.B. Actually piles never occurs, this is because:

- Too far from the portal vein to transmit pressure.
- Perianal sphincter are always in tonic contraction that compress the veins.



(Caput medusa)

Complications of portal hypertension:

6 items

- 1- Esophageal varices.
- 2- Ascites.
- 3- Portosystemic encephalopathy.

- 4- Hypersplenism.
- 5- Congestive gastropathy (bleeding)
- 6- Renal failure.

Esophageal varices :

- Dilated, elongated, tortuous veins located at lower end of the esophagus.

- **Etiology** : I can say that portal hypertension is the only cause of esophageal varices & no one can blame me !!

- **Clinical Picture** :

- Approximately 90% of cirrhotic patients will develop esophageal varices, over 10 years, but only $\frac{1}{3}$ of these will bleed.
- Bleeding is likely to occur with large varices, red signs on varices (diagnosed by endoscope) and in severe liver disease.

i- **before rupture:**

- Asymptomatic (silent)
- dysphagia (rare)

ii- **At rupture:** Upper GIT bleeding

- Painless massive hematemesis.
- Melena.

N.B. Because other etiologies of upper gastrointestinal bleeding are also common in cirrhotics (gastritis, peptic ulcer) variceal bleeding should be confirmed with endoscope (even in patient with known varices).

Investigation of portal hypertension: (esophageal varices)

6 items

1- Endoscopy:

- Detects early varices. (Esophageal varices confirm the diagnosis of portal hypertension)
- Detects signs of impending rupture (red signs).
- Detects active bleeding & its site.
- Can be used for sclerotherapy of varices.

2- Imaging of the portal circulation :

- a) Doppler or Duplex ultrasound : Detect pressure , blood Velocity & patency.
- b) CT , MRI.

3- Measurement of the hepatic venous pressure gradient : HVPG

(Free & wedged hepatic venous pressure)

- Catheter is introduced into SVC → IVC → hepatic vein (*free hepatic venous pressure*)
→ then pushed till it is wedged in hepatic sinusoids (*wedged hepatic venous pressure*)
- It is an indirect measurement that closely approximates portal vein thrombosis.

4- Spleno-portography: needle introduced into the spleen → inject dye for patency of portal vein.**5- Evaluation of the liver:** liver function tests , liver biopsy.**6- Investigations of Bilharziasis :** e.g. Barium enema.

N.B. *Direct portal measurements usually are not performed due to invasive nature.*

Treatment of portal hypertension:

- 1- Treatment of esophageal varices.
- 2- Treatment of porto-systemic encephalopathy.
- 3- Treatment of ascites.

Treatment of esophageal varices:

During attack: (Control of acute bleeding) 6 items

- 1- **Initial resuscitation** with replacement of blood volume.
- 2- **Endoscopy** to detect the site of bleeding.
- 3- **Pharmacological therapy :**

- ✎ Vasopressin.
- ✎ Somatostatin.
- ✎ **Octreotide.**
- ✎ Terlipressin.

Vasopressin: (*pitressin*)

- ✎ V.C. of mesenteric & hepatic arterioles $\Rightarrow$ $\downarrow$ Portal inflow $\Rightarrow$ $\downarrow$ portal vein pressure $\Rightarrow$ $\downarrow$ Hemorrhage.
- ✎ Dose: 20 unit in 200ml glucose 5% over 20 min.
- ✎ SE: generalized V.C may result in peripheral vascular ischemia, Ischemic heart disease & hypertension so, we may use nitrate with vasopressine.
- ✎ Somatostatin or **octreotide** are more safer.

- ✓ Whatever drug is used, it's inadvisable to continue drug therapy for more than 1 to 2 days.
- ✓ Pharmacological therapy can be initiated as soon as variceal hemorrhage is suspected, even before diagnostic endoscope.

4- Injection sclerotherapy and / or band ligation: (endoscopic therapy)

The efficacy of rubber band ligation is similar to sclerotherapy with fewer complications e.g. esophageal ulceration, stricture, chest pain, aspiration ...

5- Sengstaken- Blakemore tube : mechanical compress of esophageal varices.

➤ **Diagnostic value** :

Used in a case of hematemesis, if the bleeding doesn't stop ⇒ source is not the esophagus.

➤ **Therapeutic value** :

- If bleeding doesn't stop by conservative treatment.
- If endoscope is not immediately available.

S/E: Esophageal perforation & ischemia especially in inexperienced hand.

6- When all the above measures fail, Transjugular intrahepatic portosystemic shunt (TIPSS) or portosystemic shunt operations are considered.

Remember golden 3S : **S**omatostatin, **S**clerotherapy & **S**engstaken tube.

Prevention:

6 item (3 primary , 3 secondary)

1ry prevention (silent varices)

(Prevention of the first variceal bleeding)

- 1- Small varices: no treatment is required.
- 2- Large varices:
 - ✗ β blockers (propranolol) : ↓ COP , splanchnic vasoconstriction.
 - ✗ Nitrates (isosorbide mononitrate) : venodilator
- 3- Impending rupture: band ligation (Endoscopic Variceal Ligation , EVL)

NB : prophylactic injection sclerotherapy has no role in primary prophylaxis.

Secondary prevention

(Prevention of recurrent variceal bleeding)

- 1- β blockers (propranolol) : $\downarrow$ the risk of rebleeding up to 40%.
- 2- Repeated injection sclerotherapy or band ligation till varices disappear.
- 3- TIPS , portosystemic shunt & liver transplant are considered in patient who rebleed during above measures.

- TIPSS (transjugular Intrahepatic porto-systemic shunt):

- Inserting of short metal tube through neck vein (Jugular) $\rightarrow$ liver (hepatic) & connect portal vein with hepatic vein (porto-systemic).
- It requires only light sedation & local anesthesia.

- Porto-systemic shunts:

- * **Portocaval**. (SE : encephalopathy)
- * mesenterico caval.
- * **lienorenal** $\rightarrow$ minimal encephalopathy.
 - $\rightarrow$ 2 types : Distal (*warren operation*).
 - : proximal.
- **HASSAB operation** (minor surgery) : Splenectomy & esophageal devascularization.

Gastro-Intestinal Bleeding

Upper GIT bleeding:

- Site of bleeding: is proximal to ligament of Treitz. (*distal duodenum*)
- Presentation:
 -  Hematemesis
 -  Melena
 -  Occult blood in stool

Lower GIT bleeding:

- Site of bleeding: is distal to ligament of Treitz.
- Presentation:
 - Hematochezia (*Bleeding per rectum*)
 - Melena.
 - Occult blood in stool.

Hematemesis :

- Vomiting of blood coming from esophagus, stomach & duodenum.
- Blood may be:
 - Red in color: if immediately after bleeding
 - Coffee ground (*Melenemesis*): when blood is in contact with gastric acid for at least 1 hour.

Etiology of hematemesis :**Esophageal:**

- Esophageal varices.
- Cancer esophagus.
- Esophagitis due to infections , reflux ,..
- Mallory – Weiss syndrome :
 - Mucosal tear due to repeated vomiting.
 - Treatment : self limited, vasopressin may be used.

Gastro-duodenal:

- Duodenal ulcer.
- Gastric ulcer.
- Gastritis.
- Cancer stomach.

Systemic (general) causes:

- Hemorrhagic blood diseases.
- Hemorrhagic fever.
- Severe hypertension.
- Heparin therapy.

Diagnosis of hematemesis:

Remember this word **CIS** : **C**ause - **I**ron deficiency anemia - **S**hock 😊

1- History :

Cause	Question to detect the cause
1- Esophageal varices	History of cirrhosis, confusion?
2- Peptic ulcer	Epigastric pain, dyspepsia, heart burn?
3- Gastritis	History of drug intake e.g. Aspirin, Alcohol, NSAID? Epigastric pain?
4- Cancer stomach	Weight loss, Meat dyspepsia
5- Mallory-Weiss.	Preceded by severe vomiting?
6- Coagulation defect	Oral anticoagulant? History of cutaneous or orifice bleeding?

2- Examination :

- i. Manifestations of the cause e.g. chronic liver disease.
- ii. Manifestations of hypovolemic shock :
 - Pallor & cold sweating.
 - Low systolic BP < 100 mmHg, Tachycardia > 100/min.
- iii. Manifestations of iron deficiency anemia in a case of recurrent bleeding.

3- Investigations :

- i. Nasogastric tube: usually +ve for blood
- ii. Endoscopy to localize the site of bleeding.
- iii. Angiography : done if endoscope fails to show the site of bleeding.
- iv. Lab : CBC , Liver function tests.

Treatment of hematemesis:

- 1- Resuscitation: IV fluid & fresh blood transfusion if necessary.
- 2- Endoscopy.
- 3- Treatment of the cause: e.g.
 - Esophageal varices : see before.
 - Peptic ulcer : IV Proton pump inhibitor (omeprazole) or H₂ blocker.
- 4- Iron therapy: given in chronic cases presenting with iron deficiency anemia.

DD of hematemesis:

- Differentiation of the cause.
- Hemoptysis.
- False hematemesis : Ingestion of blood after bleeding from the nose, mouth or pharynx then vomiting of this blood.

Melena:

- Passage of **black tarry stool** due to presence of digested blood.
- It indicates that hemorrhage has remained for ≥ 8 hours in the GIT
- Site of bleeding : is not merely above ligament of Treitz as hematemesis but may extend up to the right colon. (above the ileocecal valve)

Etiology :

- i- Etiology of upper GIT bleeding (hematemesis) plus
- ii- Jejunum & ileum: 2T + 2C
 - T.B enteritis
 - Typhoid ulcer
 - Cancer head of pancreas.
 - Crohn's disease.
- iii- Colon:
 - Ulcerative colitis.
 - Right sided tumor.

DD of dark stool:

- Melena.
- Iron ingestion.
- Hemolytic Jaundice.

Diagnosis & Treatment of melena: The same as hematemesis.

Hematochezia:

- Passage of **bright red blood** per rectum.
- Usually indicate that lesion distal to right Colon.

Etiology :

- Anal lesions (Hemorrhoids, fissures).
- **Diverticulosis.**
- Polyps.
- Ulcerative colitis.
- Infectious colitis.
- Colonic Cancer: usually present with chronic occult bleeding.



Diverticulosis is the most common cause of acute lower GI bleeding in patients > 40 years of age.

Diagnosis of Hematochezia:

1. Clinical history.
2. PR examination.
3. Colonoscopy.
4. Barium enema.
5. Nasogastric tube : -ve
6. Lab : Anemia.



Avoid flexible Sigmoidoscopy and barium enema in the initial stages of diverticulitis because of perforation risk.

Occult GIT blood loss:

Normal appearing stool but hemocult +ve.

We are creatures of habit, yet we tend to compete to achieve a greater and better habit, mostly called success. But do remember a successful life lies in the way you set an example to others and how you can change their lives.

Ahmed Mowafy "Author"

HEPATITIS

Definition : is an inflammation of the liver

Etiology

Infectious

Non infectious

- * Alcohol
- * DDT – Halothan
- * Paracetamol - INH

Viral

- * 5 major hepatitis viruses: A, B, C, D, E
- * Recently F & G
- * Other viruses: **MCQ** CMV, EPV, herps simplex.

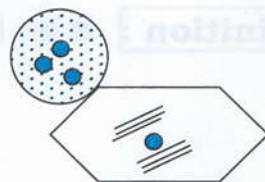
Non viral

- * Malaria
- * Leptospirosis
- * Brucellosis 🎵🎵

	A	B	C	D	E
Viral genome	RNA	DNA	RNA	RNA (incomplete virus with HBs Ag coat)	RNA
Transmission	Feco-oral	Bodily fluid : Serum (Parenteral) Semen (Sexual) Saliva Transplacental	-Parenteral - sexual : (V.rare, anal only)	Parenteral sexual	Feco-oral
IP	2-6 w	2-6 m	2-6 m	2-6 m	2-6 w
Mortality rate (fulmination)	1%	1%	0.1%	Up to 10%	1% (in pregnant women 20%)
Chronicity	No	5-10% In children : 90%	Up to 85%	50%	No
Malignancy	No	Yes	Yes	Yes	No
Prophylaxis :					
Immunoglobulin:	Non specific	Specific	-	-	-
Vaccine :	Yes (havrix)	Yes : 0,1,6 month	No	No (vaccination against HBV)	No

Pathology of acute viral hepatitis:**Hepatic pathology:**

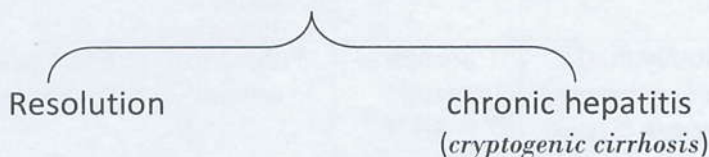
- Portal tract infiltration with inflammatory cell.
- Centrizonal necrosis & central cholestasis.
- Healthy frame work.

**Extrahepatic pathology:**

Splenomegally, lymphadenopathy, nephritis, vasculitis, bone marrow depression, arthritis.....

Clinical picture of acute hepatitis:**1- Non-icteric hepatitis:**

- Mild form of hepatitis without jaundice.
- S. bilirubin < 2.5 mg %.
- Clinically it presents by influenza like symptoms: Fever, Headache, Malaise, Anorexia (*FHMA*). So it is usually missed in diagnosis.
- Fate of not-icteric hepatitis.

**2- Icteric hepatitis:** passes through 3 stages**i- pre-icteric stage:** (*viremia*) 3-10 days.

- Acute onset of fever (*with relative bradycardia*), headache, malaise, anorexia and there may be nausea & vomiting.
- **Anorexia** is marked especially towards cigarettes & alcohol.
- Dull aching pain in Right Hypochondrium (enlarged tender liver)

ii- Icteric stage: 2-4 weeks

- Jaundice appears with improvement of general condition (↓ FHMA).
- Dark urine occurs at first followed by pale stool & then scleral ictrus.
- Jaundice is due to swelling of hepatocytes → obliteration of bile canliculi.
- Liver is enlarged, tender & soft.
- Spleen is mildly enlarged (*just palpable spleen*).
- LN : slightly enlarged cervical LN may occur in about 10% of cases.

DD of just palpable spleen:

- Hepatitis - Typhoid - Brucellosis - SBE - IMN - Grave's disease.

iii- Post icteric: (*Convalescence stage*): 3-6 months

- Symptoms & signs gradually disappear.
- S. bilirubin ↓↓ but jaundice still present for some time (*bilirubin has high affinity to collagen elastic fibers especially in sclera*).
- Within 3-6 months, patient become clinically and biochemically free.

Sequelae of hepatitis:

- i. Complete recovery
- ii. Complications

i. Complete recovery :

- All cases of HAV, HEV.
- Many cases of HBV.
- Few cases of HCV.

ii. Complications :

6 items

1- Relapse: clinical or biochemical relapse.

2- Acute fulminant hepatitis:

- Rare condition in which there is rapid development of fulminant (acute) hepatic failure (*encephalopathy & coagulopathy*).
- May develop so rapidly that jaundice is not apparent so, the condition may be misdiagnosed as encephalitis. (*details : see acute liver cell failure*)

3- Prolonged cholestasis: "watson's syndrome"

- Due to unresolved edema of hepatocytes → close bile canaliculi → jaundice deepens with pruritus.
- This condition may occur especially with hepatitis A.
- The condition resolves within 8-28 weeks.

4- Post hepatitis syndrome: *may be psychic ?*

- Here, the patient is still complaining (fatigue, anorexia & pain in Right Hypochondrium) even after recovery.
- Liver function tests & liver biopsy are normal but, transaminases may be raised (*transaminitis*).

5- Chronic complications: only in hep. B, C, D

- **C**hronic hepatitis.
- **C**irrhosis.
- **C**ancer.
- **C**arrier. (+ve hepatic markers , -ve hepatic enzymes)

6- Extrahepatic complications: (*immune complex manifestations*).**I. Hematological :**

- **Essential mixed cryoglobulinemia : (EMC)** Details : see hematology book
 - ✓ Medical condition in which the blood contains large amounts of cryoglobulins - *proteins that become insoluble at reduced temperatures*.
 - ✓ Hepatitis C can be found in 95% of all patients with EMC.
 - ✓ C/P : Rash, arthralgia, splenomegaly & muscle weakness.
 - ✓ Interferon : leads to symptomatic improvement of both rash & joint pains.
- **Lymphoma :**
 - ✓ There is an increased incidence of B cell lymphoma in patients with hepatitis C.
 - ✓ Lymphadenopathy & unexplained chronic anemia in a patient with hepatitis C infection should raise the possibility of lymphoma.

II. Renal :

- GN : The most common histological lesion is membranoproliferative GN.

III. Dermatological :

- Porphyria cutanea tarda : (PCT)

It is the most common form of porphyria. The disorder results from low levels of the enzyme responsible for the fifth step in heme production.

- Lichen planus : is a chronic mucocutaneous disease that affects the skin, tongue, and oral mucosa.

IV. Endocrine disorders :

- DM : Hepatitis C increases the incidence of type 2 DM 3 times.
- Thyroid dysfunction : due to increased antithyroid antibodies.

V. Neurological :

- Peripheral neuropathy : especially mononeuropathy multiplex.
- Encephalitis & encephalomyelitis.

VI. Eye :

- Uveitis.
- Corneal ulcer.

VII. Others :

- Sialadenitis : inflammation of salivary gland.
- Polyarteritis nodosa.
- Pancreatitis.
- Idiopathic pulmonary fibrosis.

Investigations:

6 items

1- Urinalysis : (bedside test)

- Dark frothy urine due to early appearance of bilirubin & bile salts.
- Urobilinogen is variable.

2- Stool analysis:

- ↓↓ stercobilinogen.
- Pale stool with steatorrhea.

3- **Blood picture:**

leucopenia with relative lymphocytosis due to bone marrow depression.

4- **Abdominal ultrasonography (US)** : diffuse hepatomegaly.5- **Liver function tests:**

- ALT & AST : Dramatically ↑↑.
- Serum bilirubin: ↑↑ (direct & indirect).
- Alkaline phosphatase: moderate ↑↑.
- Albumin: normal.
- Prothrombin time : Prolonged in severe cases, as all clotting factors except factor VIII are produced by the liver.

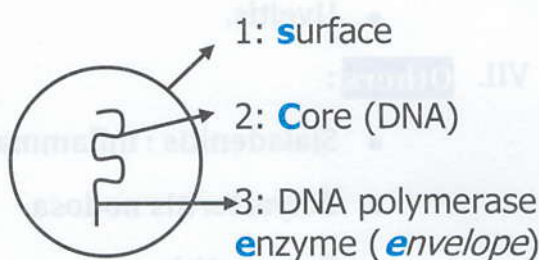
6- **Hepatitis markers:** (serology)**Hepatitis A markers:**

- HAV antigen : in stool only (*rarely used*).
- HAV antibodies: IgM → recent infection. (Ig**m** ⇒ **m**odern, **m**other ☺)
IgG → old infection (Ig**G** ⇒ **G**randmother ☺)

Hepatitis B markers:

There are 3 antigens:

- 1- HBs Ag
- 2- HBc Ag
- 3- HBe Ag



So, 3 Ag + their 3 Ab = 6 markers

HBs Ag:

First marker of infection

MCQ

- Appears in blood about **6** weeks after infection.
- Disappears after **3 - 6** months.
- If present longer than **6** months = chronic hepatitis or carrier.

HBsAb:

- Appear in blood after about 3 months & persists.
- If +ve = immune so, no need for vaccine.

Window gap (W.G): is the period () disappearance of HBsAg & appearance of HBsAb.

HBcAg:

Found only in hepatocytes & not in blood.

HBcAb: (IgM & IgG)

🔗 HBcAb IgM :

- Acute hepatitis B (*high titre*) , may be +ve during the window gap.
- Chronic hepatitis B (*low titre*)

🔗 HBcAb IgG : is a lifelong marker indicates past exposure to Hepatitis B. It does not signify immunity or previous vaccination.

HBeAg:

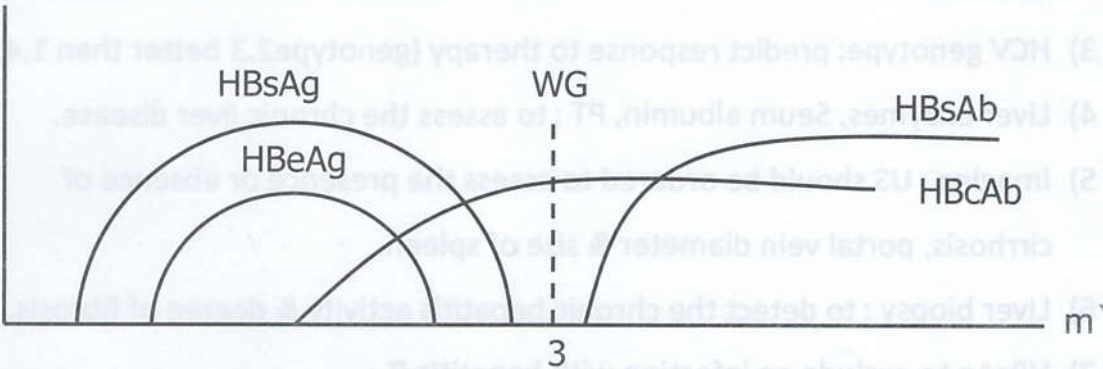
Appears shortly after HBsAg in the serum and its persistence is indicative of active viral replication and a high degree of infectivity. (**BE**ware 😊)

HBeAb: It indicates low infectivity.

What laboratory tests should be ordered to screen for acute hepatitis B infection?

HBsAg and IgM anti-HBc

MCQ



	Good prognosis	Bad prognosis
HBsAg	-ve	+ve
HBsAb	+ve	-ve
HBeAg	-ve	+ve
HBeAb	+ve	-ve

HBV DNA : by PCR: it is the most sensitive index of viral replication.

Use of HBV markers in clinical practice :

Test	Acute hepatitis B	Resolved acute hepatitis B	High-replication chronic HBV	Low-replication chronic HBV	Vaccination
<i>HBsAg</i>	+	-	+	+	-
<i>HBeAg</i>	+	-	+	-	-
<i>Anti-HBs</i>	-	+	-	-	+
<i>Anti-HBe</i>	-	+	-	+	-
<i>IgM anti-HBc</i>	+	-	+	-	-
<i>IgG anti-HBc</i>	-	+	+	+	-
<i>HBV DNA</i>	>10 ⁵ copies/milliliter	Negative	>10 ⁵ copies/mL	10 ² - 10 ⁴ copies/mL	Negative
<i>ALT/AST</i>	+++	Normal	+++	Normal	Normal

Hepatitis C markers: Diagnosis of hepatitis C :

1) Anti-HCV IgM, IgG by :

- **ELISA** (enzyme-linked immunosorbant assay) : +ve after 6 wks of infection.
- **RIBA** (recombinant immunoblot assay) : to confirm +ve anti-HCV ELISA in patients with undetectable HCV RNA.

2) HCV RNA (PCR, polymerase chain reaction) : +ve within 2 wks, marker of active infection.

3) HCV genotype: predict response to therapy (genotype 2,3 better than 1,4)

4) Liver enzymes, Serum albumin, PT : to assess the chronic liver disease.

5) Imaging : US should be ordered to assess the presence or absence of cirrhosis, portal vein diameter & size of spleen.

6) Liver biopsy : to detect the chronic hepatitis activity & degree of fibrosis.

7) HBsAg to exclude co infection with hepatitis B

Hepatitis D markers: - HDV antibodies: IgM, IgG. - HBsAg: +ve.

Hepatitis E markers: HEV antibodies: IgM, IgG.

Treatment : 6 items (3 prevention, 3 therapeutic)

I- Prevention:

1- General measures:

- Hygienic measures especially in hepatitis A,E.
- Supervision of blood transfusion especially in hepatitis C, B, D.

2- Immunoglobulins: as soon as possible after exposure.

3- Vaccine:

- HAV → Havrix.
- HBV → hepatitis B vaccine (0, 1, 6, m'), given to groups at high risk:
 - **H**ealth professionals (doctors, nurses).
 - **H**omosexuals.
 - **H**emodialysis patients.
 - **H**emophiliacs: patient requiring repeated transfusions.
 - **H**ousehold contacts of HBV patients.

II- Therapeutic treatment:

1- Rest: until the patient becomes clinically & biochemically free (bilirubin < 1.5 mg%)

2- Diet:

- Highly appetizing diet.
- CHO : ↑.
- Proteins: free but should be restricted if manifestations of LCF appear.
- Fat : low fat diet is preferred (nauseating).
- Multi vitamins.
- Alcohol: No.

3- Symptomatic treatment:

- ✗ Anti-emetics : for nausea & vomiting.
- ✗ Cholestyramine : for itching.
- ✗ Treatment of complications: e.g. acute fulminant hepatitis.

Cortisone is contraindicated, but may be indicated in a case of prolonged cholestasis.

Chronic hepatitis

Chronic hepatitis is defined as any hepatitis persisting for longer than 6 months.

Etiology:

- 1- Infections: viral hepatitis (B.C.D).
- 2- Immune: autoimmune (lupoid) hepatitis.
- 3- Iatrogenic: Alcohol, methyldopa, INH.
- 4- Inherited: Wilson's disease, α 1 antitrypsin deficiency.

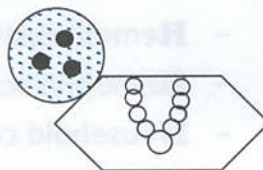
Types:

- Chronic persistent hepatitis (mild form).
- Chronic active hepatitis (severe form).

Chronic persistent hepatitis mild form

Pathology:

- It's a benign inflammatory reaction characterized by just infiltration of the portal tract by inflammatory cells.
- No loss of architecture.



Clinical picture:

- Asymptomatic: discovered accidentally &
- May be non specific symptoms: fatigue, anorexia.
- Liver may be mildly enlarged & tender.
- No cirrhosis.

Investigations:

- Liver function tests: are often normal except for elevated transaminases.
- Biopsy: to exclude chronic active hepatitis.
- Investigations for the cause : hepatitis markers.

Treatment:

- Because of its benign nature, treatment is not indicated.
- Just reassurance & follow up / 6 months.

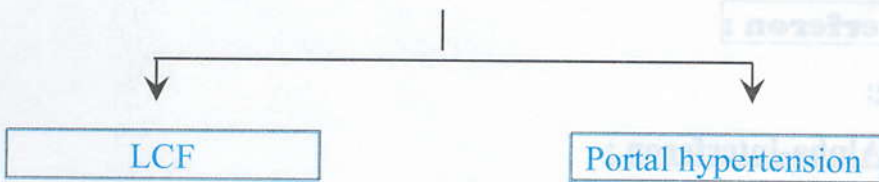
Chronic Active hepatitis

Clinical picture :

- It's mainly viral or autoimmune.
- Progression to cirrhosis is common.

Viral :

- More common in ♂.
- May be asymptomatic for decades , fatigue is a common symptom.
- Features of hepatitis : Anorexia , Jaundice , tender liver
- Features of chronicity (late) = (features of liver cirrhosis)



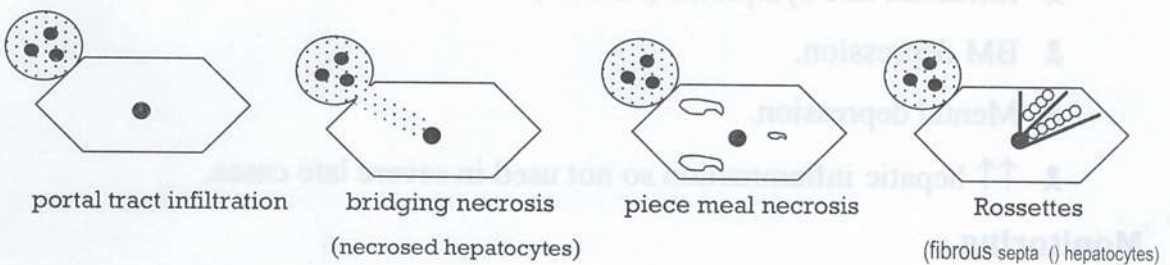
Auto Immune (lupoid hepatitis)

The same as viral but :

- more common in ♀. ☺
- some associated manifestations may be present as Hashimoto's thyroiditis , Hemolytic anemia , Polyarthritis , Pleurisy.

Investigation:

i- Biopsy : is diagnostic.



Liver cirrhosis

ii- Liver function tests:

- SGOT, SGPT : ↑ 3-5 folds.
- Serum bilirubin : ↑ (direct & indirect).
- Alkaline phosphatase : ↑ moderately.
- Albumin : ↓
- Hepatitis markers for hepatitis B, C, D : see before
- **ANA, anti smooth muscle Ab, Anti LKM-1 Ab** (Anti Liver Kidney Ab) in autoimmune hepatitis. **MCQ**

In alcoholic hepatitis, the AST:ALT ratio is usually 2:1 and the level of AST is usually < 300

Treatment:**I- Treatment of chronic active viral hepatitis:****1-Interferon :****dose:**✎ **Alpha-interferon :**

- **HBV** : 5 million units SC 3 times/week for at least 3 months.
- **HCV** : 3 million units SC 3 times/week for at least 6 months.

✎ **Peginterferon** (Peg interon) : **Long acting Interferon**

180 µg SC , once/week for at least 6 months.

Side effects:

- ☠ Expensive.
- ☠ Initial response is 50% of cases.
- ☠ Relapse occur in 50% of cases.
- ☠ Influenza like symptoms (FHMA).
- ☠ BM depression.
- ☠ Mental depression.
- ☠ ↑↑ hepatic inflammation so not used in severe late cases.

Monitoring :

- 1- PCR : If no response after 3 months : stop the drug
- 2- CBC : Stop the drug if WBCs < 3000 or platelets < 100000 /cmm
- 3- The patient must be monitored carefully for side effects including : flu-like symptoms, depression, BM depression, ...

Indications :

- HCV RNA : +ve
- Biopsy with chronic hepatitis.
- Compensated liver disease.
- For genotype 2,3 : High response rate, here, biopsy is not necessary.

Contraindications :

- Decompensated cirrhosis.
- Pregnancy.
- Psychic disorder.
- Severe cardiac or pulmonary disease.
- Uncontrolled DM.
- Seizure.
- Autoimmune disease.
- Renal failure is absolutely contraindicated for ribavirin.

2-Other antiviral agents:**✎ Ribavirin**

- 400 mg twice daily, oral, is added to interferon for HCV. (*good response*)
- Renal failure is an absolutely contraindication for ribavirin.

✎ Lamivudine : is added to interferon for HBV.

3- Recent treatment of hepatitis C :

- The goal of therapy :
 - Prevent the complications e.g. cirrhosis, HCC & extrahepatic complications
 - Improve quality of life
 - Prevent transmission of HCV
- **HCV genotype 4, without cirrhosis or with compensated (Child-Pugh A) cirrhosis should be treated with one of the following :**
 - The fixed-dose combination of **sofosbuvir** (400 mg) and **Velpatasvir** (100mg) in a single tablet once daily for 12 weeks.
 - The fixed-dose combination of **sofosbuvir** (400 mg) and **ledipasvir** (90mg) in a single tablet once daily for 12 weeks.

- The endpoint of therapy is undetectable HCV RNA in serum by a sensitive assay (lower limit of detection < 15 IU/ml) 12 weeks or 24 weeks after the end of treatment.
- In patients with advanced fibrosis and cirrhosis, surveillance for HCC must be continued.

II- **Treatment of autoimmune hepatitis:**

- **Prednisolone** :
 - 1st week : 30 mg/d then maintenance dose 15 mg/d for 6 months - 3 years.
 - If full remission → withdraw drug slowly.
 - If no remission → add **Azathioprine** (Immunar) 50 mg/d
- Treatment of the manifestations of liver cirrhosis e.g. ascites as immunosuppressive drugs have no benefit at this stage.

III. **Liver transplantation :**

May be indicated in viral & autoimmune hepatitis, but disease recurrence is frequent.

A doctor must work eighteen hours a day and seven days a week. If you cannot console yourself to this, get out of the profession.

Martin H. Fischer

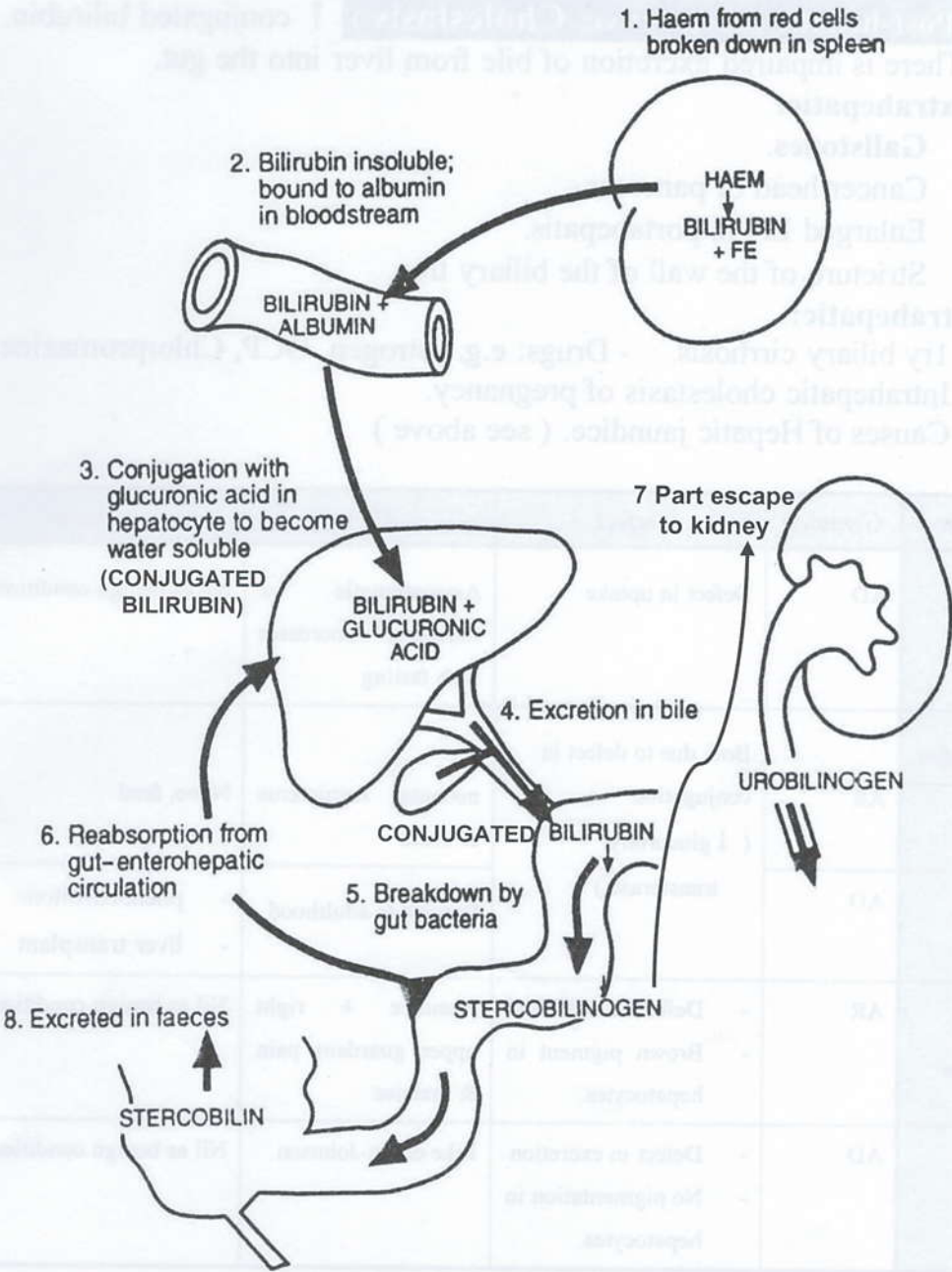
Jaundice

Derived from French word meaning yellow

Definition:

Yellowish discoloration of the skin, sclera & mucous membrane due to $\uparrow$ serum bilirubin $> 3\text{mg \%}$ ($N = 1\text{mg\%}$)

Life story of bilirubin:



Causes of Jaundice:**I- Pre-hepatic :** (↑ unconjugated bilirubin)

- Excess production of bilirubin or failure of uptake or conjugation in the liver.

- **Hemolysis (Hemolytic Jaundice).**
- Glibert's syndrome.
- Grigler- Najjar syndrome.

II- Hepatic (Hepatocellular): ↑ both conjugated & unconjugated bilirubin.
(Defect is at level of hepatocyte)

- All causes of liver cell failure e.g. viral or drug induced hepatitis.
- Dubin-Johnson & Rotor syndromes : ↑ conjugated bilirubin.

III- Post-hepatic (obstructive, Cholestasis): ↑ conjugated bilirubin.
There is impaired excretion of bile from liver into the gut.**- Extrahepatic:**

- **Gallstones.**
- Cancer head of pancreas.
- Enlarged LN in portahepatis.
- Stricture of the wall of the biliary tree.

- Intrahepatic:

- Iry biliary cirrhosis. - Drugs: e.g. estrogen, OCP, Chlorpromazine.
- Intrahepatic cholestasis of pregnancy.
- Causes of Hepatic jaundice. (see above)

Syndrome	Genetics	Defect	C/P	Treatment
<i>Glibert's</i>	AD	Defect in uptake	Asymptomatic ± Jaundice, increases with fasting	Nil as benign condition
<i>Grigler-Najjar</i>	AR	Both due to defect in conjugation (↓ glucuronyl transferase)	neonatal kernicterus & death	None, fatal
<i>Type I</i>			Survive to adulthood	- phenobarbitone - liver transplant
<i>Type II</i>	AD			
<i>Dubin-Johnson</i>	AR	- Defect in excretion - Brown pigment in hepatocytes.	Jaundice ± right upper guardant pain & malaise	Nil as benign condition
<i>Rotor</i>	AD	- Defect in excretion - No pigmentation in hepatocytes.	Like dubin-Johnson	Nil as benign condition

	Hemolytic jaundice	Obstructive Jaundice (cholestatic j)	Hepatocellular Jaundice
Pathogenesis	- ↑ hemolysis of RBCs → ↑ hemobilirubin. - The liver can't uptake hemobilirubin completely, so part of it is retained in the blood → ↑ serum bilirubin → jaundice. - Large part of hemobilirubin is converted into conjugated bilirubin & excreted by i liver→ ↑ stercobilinogen→dark stool. - Also ↑ stercobilinogen → ↑ urobilinogen which is colorless So urine is normal in color (acholuric jaundice).	- ↓ excretion of conjugated bilirubin into intestine due to obstruction → ↓ stercobilinogen → pale stool. - Conjugated bilirubin regurgitates into the blood → ↑ serum bilirubin → Jaundice. - Conjugated bilirubin is water soluble so appears in urine → dark urine N.B.: - ↓ bile excretion into intestine → steatorrhea. - Bile salts regurgitate into blood & appear in urine.	- ↓ uptake, ↓ conjugation, ↓ excretion of bilirubin. - ↓ uptake → ↑ unconjugated bilirubin. - ↓ excretion → ↑ conjugated bilirubin → dark urine. - ↓ excretion → ↓ stercobilinogen → pale stool. N.B: In HC. Jaundice: ↓ ↓ enterohepatic circulation of stercobilinogen so, urobilinogen is increased inspite of ↓ ↓ stercobilinogen.
investigations	1- In serum: ↑ unconjugated bilirubin. 2- In stool: ↑ stercobilinogen. 3- In urine: ↑ urobilinogen : Bilirubin is absent N.B: Bilirubin never > 5mg% in Haemolytic Jaundice as long as liver is normal.	1- In serum: ↑ conjugated bilirubin ↑↑ cholesterol. ↑↑ alk. Phosphatase. 2- In stool: ↓ ↓ stercobilinogen. 3- In urine: ↓ urobilinogen : Bilirubin is present	1- In serum: ↑ both conjugated & unconjugated bilirubin. 2- In stool : ↓ stercobilinogen. 3- In urine: ↑ urobilinogen : Bilirubin is present
Clinical picture	1- Jaundice: mild (lemon yellow) 2- Urine: Normal 3- Stool: dark 4- Features of hemolytic anemia	1- Jaundice: deep (<i>olive green</i>) 2- Urine: dark 3- Stool: v.pale 4- Other features of obst. Jaundice: - Steatorrhea. - Pruritis - xanthelasma - Bradycardia - bleeding - Bone affection: osteomalacia - Prolonged cholestasis → cirrhosis	1- Jaundice: orange yellow. 2- Urine: dark 3- Stool: pale 4- Features of liver failure.

How to reach a diagnosis of a case of jaundice?

I- History taking

II- Physical examination

III- Investigation

I. History taking:

Personal history:-

➡ Age :

- Child: hemolysis.
- Adult: hepatitis.
- Old: cancer head of pancreas.

➡ Sex :

- ♂ : Cancer head of pancreas, hepatitis.
- ♀ : Stones

➡ Habit : e.g. : Alcohol → hepatitis

Complaint:

Yellowish discoloration of skin & mm.

Present History:

1- Onset:

- **Acute**: hepatitis, stone.
- **Gradual**: malignant obstruction, cirrhosis.

2- Course:

- **Progressive**: malignant obstruction.
- **Regressive**: hepatitis.
- **Intermittent**: Stone.

3- Duration:

- **Short** : hepatitis.
- **Long** : cirrhosis & exclude malignancy.

4- Urine:

- **Dark** : obstructive & hepatocellular jaundice
- **Normal**: Hemolytic Jaundice.

5- Stool:

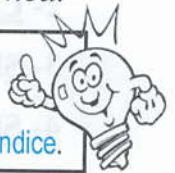
- **Dark** : hemolytic Jaundice.
- **Pale**: obstructive & hepatocellular Jaundice.

Stool in obstructive Jaundice is very pale with features of steatorrhea.

Just remember one word : **the urine is not dark in hemolytic jaundice.**

Repeat it 3 times daily

The urine is not dark, so the stool is dark ..& the opposite in obstructive & hepatocellular jaundice.

**6- Fever:**

- Hepatitis (pre icteric phase)
- Low grade fever in cirrhosis, malignancy.

7- Vomiting:

- Early viral hepatitis.

8- Pain:

- Right hypochondrium radiate to right shoulder → stone.
- Epigastric pain radiate to back → cancer head of pancreas.

9- Pruritus:

- Obstructive Jaundice.

10- Marked loss of weight: malignancy.**Past history:**

- Hemolytic crisis
- History of drug intake.
- History of biliary colic.
- History of hepatitis & bilharziasis.

Family history:

- Hemolysis.
- Gilbert's syndrome.

II- **Physical examination:**

a) General manifestations:

1- Color of Jaundice:

- Hemolytic: Lemon yellow
- Obstructive: olive green.
- Hepatocellular: Orange yellow

2- Cachexia: in malignancy

3- Skin manifestations of hemolytic Jaundice: leg ulcers

4- Skin manifestations of obstructive Jaundice: Itching, xanthlasma

5- Skin manifestations of Hepatocellular Jaundice (LCF):

6- Skin pigmentation & clubbing: in 1ry biliary cirrhosis.

7- Subcutaneous hemorrhage (Ecchymosis):

- Hepatocellular : due to ↓coagulation factors.
- Obstructive Jaundice : due to ↓ absorption of vit.k.

b) Abdominal examination:

1- Liver:

- Enlarged, soft & tender: viral hepatitis.
- Firm with sharp border: cirrhosis.
- Enlarged, hard, tender & nodular : malignancy.

2- Spleen: enlarged in hemolytic anemia, cirrhosis, hepatitis.

3- Ascites:

- Liver cell failure
- Cancer head of pancreas.

4- gall bladder: (*Courvoisier's law*)

- In obstructive Jaundice:

- Stone: **non palpable** gall bladder. (*due to fibrosis*)
- Cancer: **palpable** gall bladder.

III- Investigations:

5 Lab, 5 imaging, 5 instrumental

3 x **a) Laboratory investigations:****1- Liver function tests :**

	<i>Unconjugated bilirubin</i>	<i>Conjugated bilirubin</i>	<i>SGOT & SGPT</i>	<i>Alk. Phosph.</i>	<i>Stercobilinogen</i>	<i>urobilinogen</i>
<i>Hemolytic</i>	↑↑	normal	normal	normal	↑	↑
<i>Hepatocellular</i>	↑	↑↑	↑↑↑	↑	↓	↑
<i>Obstructive</i>	normal	↑↑	Normal or ↑	↑↑↑	↓	↓

2- Blood picture: features of hemolytic anemia.**3- ESR:** marked ↑↑ in malignancy.**4- Serological tests:** Hepatitis markers, autoantibodies.**5- Therapeutic test:**

- Vit K injection to differentiate between obstructive & hepatocellular jaundice : Vit K corrects the prothrombin time in obstructive Jaundice, not in hepatocellular Jaundice.
- Cortisone test : to differentiate between intra & extra cholestasis.

Isolated hyperbilirubinemia :

(↑ bilirubin, normal AST & ALT, and alkaline phosphatase).

I. Unconjugated :

- Hemolytic anemia. (overproduction)
- Gilbert's syndrome.
- Crigler-Najjar syndrome.

II. Conjugated : Dubin-Johnson-Rotor syndrome.**B- Imaging:****1- x-ray:** gall stones.**2- Barium:** - Swallow: esophageal varices.

- Meal: wide C duodenum in cancer head of pancreas.

3- U/S**4- CT****5- Isotopic scan**

C- Instrumental:

- 1- **ERCP**: (*Endoscopic Retrograde Cholangio – Pancreatography*) is used to investigate obstructive Jaundice & remove obstructing gallstones.
- 2- **PTC**: (*percutaneous Transhepatic Cholangiography*) indicated in obstructive Jaundice with intrahepatic biliary dilatation.
- 3- **Liver biopsy**: after correction of bleeding tendency.
 - Technically difficult if ascites is present.
- 4- **Laparoscopy**.
- 5- **Laparotomy**.

Treatment of Jaundice:

Since Jaundice is a symptom, not a specific disorder, treatment for it **depends on its cause**. This can range from the removal of gall stones or tumors to antibiotics to treat infections, to liver transplant in cases where the liver is severely damaged. However, for conditions like cirrhosis & chronic hepatitis, which are lifelong problems, Jaundice may be permanent or recurrent.

N.B: Causes of recurrent Jaundice:

- 1- Hemolytic crisis
- 2- Gall stones → recurrent obstructive Jaundice.
- 3- Recurrent hepatitis.
- 4- Recurrent cholestasis of pregnancy.
- 5- **Drug induced Jaundice:-**

- **Hemolytic:**

- Drug caused hemolysis: sulpha, α methyl.dopa.
- Rifampicin: $\downarrow\downarrow$ uptake of bilirubin.

- **Hepatocellular:**

- **DDT**, **Halothan**, **paracetamol** – **INH**

- **Obstructive:**

- **Anabolic steroid**, **PAS**, **chlorpromazine**, **Dindivan**, **Erythromycine**

POST OPERATIVE JAUNDICE :

Definition : Jaundice occurring for the first time in the post operative period.

Etiology :

a) Unconjugated hyperbilirubinemia :

- 1- Massive blood transfusion or mismatched blood.
- 2- Absorption of residual hematomas.

b) Hepato-cellular damage :

- 3- Septicemia
- 4- Drug induced liver jaundice e.g. Halothane.
- 5- Viral hepatitis.
- 6- Activation of pre-existing liver disease.

c) Extra-hepatic obstruction :

- 7- Missed stones.
- 8- Post operative pancreatitis.
- 9- Injury to the common bile duct.
- 10- Sclerosing cholangitis.

Sclerosing cholangitis :

- Term used to describe fibrous thickening of the bile duct wall associated with multiple strictures.
- It may occur secondary to congenital lesion , operative trauma or no etiology is evident (*1ry sclerosing cholangitis*)

	Intra-hepatic cholestasis	Extra-hepatic cholestasis
I . History : ○ Drugs & alcohol: ○ Viral hepatitis : ○ Pain : ○ Duration :	+ + - Usually long	- - + Usually short
II. Examination : ○ Liver size : ○ Spleen : ○ G.B. : ○ Ascites :	± ± - ±	+++ - ± -
III. Investigation : ○ US : ○ Cortisone test :	Constriction of intra-hepatic bile radicals. +	Dilation of intra-hepatic bile radicals. -

	Calcular obstruction	Malignant obstruction
I. History : ○ Age & sex : ○ Onset : ○ Course : ○ Duration : ○ Pain :	Female , 40 Y Acute Intermittent Long Colicky in the right hypochondrium radiating to the right shoulder.	Male , 60 Y Gradual Progressive Short Epigastric pain radiating to the back , relived when the patient lies on his belly & exaggerated when the patient lies on the back.
II. Examination : ○ General : ○ Liver : ○ G.B. : ○ Ascites : ○ Abdominal mass :	Moderate state Enlarged , smooth Usually not enlarged - -	Bad state , loss of weight Enlarged , may be nodular. Usually enlarged In late cases May be felt .
III. Investigations : ○ Amylase	-	+++

Hepatic Bilharziasis

Etiology :

S. mansoni is responsible for 85% of cases, while *S. hematobium* is responsible for 15%.

Life cycle :

Adult worm in portal vein ⇨ *Ova in urine or stool* ⇨ *miracidia in water* ⇨ *sporocysts in snails* ⇨ *cercaria in water* ⇨ *infect man by skin penetration* ⇨ *circulatory system* ⇨ *adult worms in portal vein*.

Pathogenesis:

Ø Ova reach liver through portal vein tributaries



Lodged in portal tracts



These ova induce cell mediated immune reaction with formation of granuloma (ova surrounded by lymphocytes, macrophages & eosinophils)



Periportal fibrosis.



Pre-sinusoidal portal hypertension.

In pure B → Liver fibrosis & not cirrhosis. (Patients with B usually develop cirrhosis mostly due to post hepatitis cirrhosis).

Clinical picture :

4

- 1- History of Bilharzial dysentery (.....)
- 2- Portal hypertension (.....)
- 3- Liver cell failure → very rare as the hepatic architecture is normal in pure bilharziasis. It may occur in mixed pathology e.g. hepatitis C.
- 4- Pulmonary hypertension & cor-pulmonale may be present.

Characteristic facies :

- i. Wasted dehydrated in upper part of the body , while ascites in mid and edema of lower limbs (*spider man*).
- ii. Parotid enlargement , anemia due to malnutrition, bleeding & hypersplenism.
- iii. Jaundice : very rare & mild.

Liver : Enlarged liver in early cases, NOT tender (*except in associated hepatitis or amebic abscess*), NOT nodular. Later on become shrunken.

Spleen : Enlarged and may reach a huge size : first due to reticulo-endothelial hyperplasia and later due to portal hypertension.

Ascites : may develop late due to associated hypoalbuminemia.

Causes of associated hypoalbuminemia

1. Decreased intake : nutritional deficiency.
2. Decreased absorption : Malabsorption due to intestinal congestion.
3. Decreased production : due to associated cirrhosis in mixed pathology.
4. Increased loss : Bleeding, Protein losing enteropathy.

Stages of hepatic bilharziasis : 4 stages

- 1-Hepatomegaly.
- 2-Hepatosplenomegaly.
- 3-Shrunken liver & splenomegaly.
- 4- Shrunken liver, splenomegaly & ascites.

Investigation:

- 1- Investigations to detect bilharziasis (see Bilharzial dysentery)
- 2- Investigations for portal hypertension
- 3- Liver function tests: +ve if there is mixed pathology in the liver.
- 4- Investigation for pulmonary corpulmonale: X ray, echo

Treatment:

- 1- Anti B (see B dysentery)
- 2- Treatment of portal hypertension.
- 3- Treatment of liver cell failure.
- 4- Treatment of corpulmonale.

Amoebic liver abscess

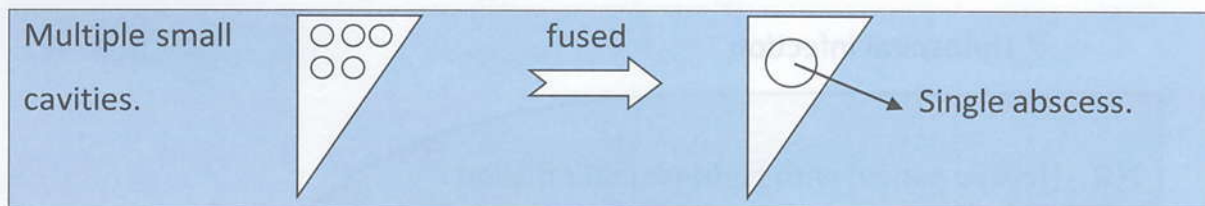
(Amoebic Hepatitis)

Etiology:

- Entamoeba histolytica (*vegetative form*) reaching the liver from the colon through portal vein.
- Amoebic dysentery is present in only 50% of cases.

Pathogenesis:

Amoeba reaches liver through portal vein tributaries → foci of necrosis.



Contents of the abscess :

Necrotic tissue + RBC ± pus cells with 2ry infection (*Anchovy Sauce* – chocolate material)

Clinical picture :



1- History of amoebic dysentery. (.....)

2- Features of hepatitis : but there are :

- Severe toxemia : fever with rigor, toxic face.
- The liver is enlarged & **tender**.
- Jaundice is usually **absent** & if present, it's due to obstruction of bile ducts by the abscess.

Don't forget : 3Ps

Pyrexia.

Pain.

Pleural effusion.

3- Complications : spread & rupture

- **Right p**leural effusion, lung abscess.
- **P**ericarditis.
- **p**eritonitis.
- Cutaneous amoebiasis.

DD:

i- **Causes of enlarged tender liver :**

- * Inflammation: all except Bilharziasis , Syphilis.
- * Malignancy (if capsule is infiltrated).
- * Hepatic congestion.
- * Cholestasis.

ii- Fever of unknown origin.

iii- ~~DD~~ Of Jaundice with leucocytosis

- * Amoebic liver abscess. * Ascending cholangitis.
- * Liptospiral infection

NB : Hepatic patient with **right** pleural effusion :

- * Amoebic hepatitis .
- * Ascites.

Hepatic patient with **left** pleural effusion $\Rightarrow$ T.B.

Investigation:

1- Investigations to detect Amoeba: **4S** (See amoebic dysentery)

2- Liver function tests:

- Usually normal, Amoebic hepatitis is a focal lesion.

- **Alkaline phosphatase** : $\uparrow\uparrow$

3- US & aspiration of abscess.

4- Blood picture: Leucocytosis.

5- Chest X-ray:

- Raised right copula of diaphragm.
- Pleural complications may be detected.

6- Therapeutic test : Metronidazole is given & response is detected.

Treatment:**I- Medical treatment:****1- Antiameobic drugs:** (see Amoebic dysentery)

Metronidazole (Flagyl): 750mg t.d.s for 10 days + chloroquine (250mg twice daily) for 3 weeks + Iodoquinol (Entocid).

2- General care:

- Rest.
- Light nutrient diet.

3- Symptomatic treatment: analgesics & antipyretics.**4- Treatment of complications:** Antibiotics for 2ry infections.**II- Aspiration:** In cases not responding to medical treatment.**III- Surgical drainage:** indicated in:

- Huge abscess.
- Multiple abscesses.
- Cases not responding to medical treatment & aspiration.

"Internal Medicine impulse through the mind"

Dr.Mohamad Rashed IRIS ASPECT founder, Doctor

Addiction-Free Nation Program should consider **in capsule series** its 1st priority, as it has been proved that almost all internal medicine seekers are addicted to it.

Alainy School of medicine, Doctor

Dr. Alsayed Dawoud Kasr-

Hepatoma

(Hepatocellular carcinoma)

- It's highly malignant tumor, from the time of presentation → death within < 6 months.

Predisposing factors:

- 1- Age: Usually > 40 y.
- 2- Sex: ♂ > ♀ 3 times.
- 3- Hepatitis: HBV, HCV.
- 4- Cirrhosis: especially haemochromatosis.
- 5- Aflatoxins: mycotoxins secreted from saprophytic fungi on stored grains.

N.B: Contraceptive pills → adenoma not hepatoma.

Clinical picture: (when do u suspect hepatoma in hepatic patient?)

- 1- Rapid unexplained deterioration of his condition : encephalopathy, loss of weight.
- 2- Right hypochondrial pain or appearance of local swelling.
- 3- Resistant ascites.

4-**Paramalignant syndrome** : (non metastatic manifestations)

- Endocrinal :

Due to abnormal peptides secreted from the tumor which may be similar to hormones :

- Insulin like peptide → hypoglycemia.
- Parathormone hormone → ↑ Ca.
- ACTH like peptide → Cushing's.

- CNS : Polyneuropathy , myopathy , myasthenia .
- Cutaneous : acanthosis nigricans , dermatomyositis.
- Cachexia , clubbing.

Investigation :

1- Hepatoma markers:

i - α fetoprotein: $\uparrow\uparrow$ in 65% of cases. (> 2000 ng%)

ii- Corboxy prothrombin.

2- Hepatic scanning: CT, MRI, US.

3- Portal venography: portal vein thrombosis.

4- Hepatitis B &/or C markers: usually + ve.

5- Liver biopsy $\rightarrow$ diagnostic, but better avoided.

Treatment:

1-Medical: Systemic or local cytotoxic chemotherapy (adriamycin) "unsatisfactory"

2- Surgical resection : This is the treatment of choice for non-cirrhotic patients.

3-Hepatic embolization: injection of gel foam in blood supply of tumor.

4- Radiofrequency ablation.

5 -Hepatic transplantation.: the result is unsatisfactory.

Liver transplantation

A liver transplant is a surgical procedure to remove a diseased liver and replace it with a healthy liver from a donor.

Indications : 6

1. Liver cirrhosis of all causes with poor liver function e.g. Child-Pugh C, Hepatorenal syndrome, primary biliary cirrhosis.
2. FHF (Fluminant hepatic failure).
3. Budd- chiari syndrome.
4. Hepatocellular carcinoma.

5. Biliary atresia (*failure of bile duct formation*) : is the most common indication in children. **MCQ**

6. Inherited disorders of metabolism :

- Glycogen storage diseases.
- Tyrosinemia.
- α 1-Antitrypsin deficiency.
- Familial hypercholesterolemia.
- Crigler-Najjar disease type I
- Wilson's disease.
- Hemochromatosis.

Contraindications :

I. Absolute :

1. Severe systemic illness.
2. Uncontrolled sepsis.
3. Extrahepatic malignancy.
4. Advanced cardiopulmonary disease.
5. AIDS.

II. Relative :

- Age > 70
- Portal vein thrombosis.
- Hepatoma more than 3cm in diameter.
- Renal failure.
- Severe obesity or malnutrition.
- Uncontrolled psychiatric disorder.

Complications : 6

1. Liver graft rejection : acute or chronic rejection.
2. Hepatic artery thrombosis, biliary obstruction or leak.
3. Postoperative bleeding.
4. Postoperative infections, recurrent hepatitis.
5. Postoperative malignancy : lymphoma, hepatoma.
6. Renal dysfunction : Hypoperfusion injury, Drug nephrotoxicity.

Surgical technique :**1. Orthotopic liver transplantation :**

- The native liver is removed and the donor organ is inserted into the same location. In this case, the liver donor is someone who has recently died.
- During the anhepatic phase, coagulopathy, hypoglycemia, hypocalcemia, and hypothermia must be managed by the anesthesiology team. Large volumes of blood and volume expanders may be required during surgery.
- A typical transplant operation lasts 8 h, with a range of 6 to 18 h.

2. Auxiliary transplantation : The patient's liver is NOT entirely removed.**3. Split liver transplantation :** The liver of the donor is split into 2 pieces to supply 2 patients.**4. Living donor liver transplantation (LDLT) :** part of the liver (usually right lobe) of the patient's relative is transplanted.

Immunosuppressive drugs : Cyclosporine, Predinsone, Mycophenolate.

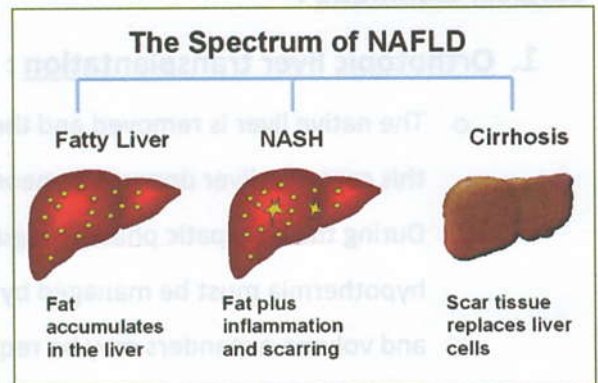
Liver donor requirements : The criteria for a liver donation include:

- Good health.
- Compatible blood group and organ size between donor and recipient.
- Having a charitable desire of donation without financial motivation.
- Being between 18 and 60 years old.
- Should be negative for HIV, HBV, and HCV.

Non Alcoholic Fatty Liver Diseases (NAFLD)

Definition :

- It is one cause of fatty liver in which there is a fat deposition in hepatocytes, not due to excessive alcohol use.
- It is becoming now one of the **most** common causes of chronic liver damage worldwide.
- **Steatosis** (*simple fatty liver*) : Fatty infiltration without inflammation.
- **Steatohepatitis** (*Non Alcoholic Steato-Hepatitis, NASH*) : Steatosis with inflammation that may lead to progressive fibrosis & cirrhosis.



Etiology :

a) Primary : Idiopathic.

b) Secondary :

- **Insulin resistance** associated with type II DM.
- **Obesity.**
- **Metabolic syndrome.**
- Hypertriglyceridemia.
- Malnutrition & rapid weight loss.
- Surgical : Gastric & jejunioileal bypass.
- Wilson's disease.
- Drugs & toxins :
 - ☠ Amiodarone.
 - ☠ Aspirin (rarely as part of Reye's syndrome in children).
 - ☠ Pesticides.
 - ☠ Cortisone.
 - ☠ Chloroquine.

☒ Methotrexate.

Pathogenesis :

- The pathogenesis of NAFLD is still *unclear*. Hepatic steatosis is due to lipid accumulation, mainly of triglycerides, within hepatocytes.
- Accumulation of hepatic fat is closely linked to insulin resistance, which increases lipolysis of peripheral adipose tissue with resultant increased fat influx into the liver in the form of free fatty acids.
- The injury may be due to direct cellular toxicity of excess free fatty acids, oxidant stress or lipid peroxidation.

Clinical picture :

- Usually asymptomatic.
- Pain, heaviness & discomfort in the right hypochondrium.
- Palpation : enlarged liver with a smooth surface & soft to firm consistency.

Investigations :

I. **L**ab :

- Elevated ALT and AST.

*There is **no relation** between the degree of ALT elevation & the histological severity of steatosis or fibrosis.*

- Bilirubin, albumin and prothrombin time are usually not affected in fatty liver disease until cirrhosis and liver failure develop.
- Lipid profile : hypertriglyceridemia and/or elevated low-density lipoprotein (LDL)

II. **L**iver imaging : US, CT, MRI.

III. **L**iver biopsy is the gold standard for diagnosis. It is the only way to confirm the presence or absence of NASH.

Diagnosis of NAFLD/NASH :

- Involves history-taking to exclude significant alcohol intake.
- Involves the exclusion of other possible causes of abnormal liver tests e.g. absence of serological evidence of viral hepatitis.
- Consider **liver biopsy** for diagnostic and prognostic purposes.

Treatment :

1. Lifestyle modifications :

- Exercise (30 minutes thrice weekly) and dietary modifications.
- Reduce sedentary lifestyle.
- Avoid too rapid weight loss ($>1.6\text{kg/week}$).

2. Pharmacologic therapy :

- Insulin sensitizers : Thiazolidinediones, metformin.
- Anti-oxidants : e.g. vit E to decrease the oxidant stress induced by accumulating lipid.
- Ursodeoxycholic acid (UDCA) and lipid-lowering drugs.

3. Surgical therapy :

- Bariatric surgery for patients with $\text{BMI} > 32.5\text{kg/m}^2$ with co-morbidities or $\text{BMI} > 37.5\text{ kg/m}^2$ without co-morbidities.
- Liver transplantation in a patient with decompensated NASH cirrhosis.

Ascites

The word ascites is of Greek origin (askos) and means sac

Definition :

- Excessive accumulation of fluid in peritoneal cavity. Healthy men have little or no intraperitoneal fluid, but women may normally have as much as 20 ml depending on the phase of menstrual cycle.

Causes:

I. Transudative ascites :

a) Increased hydrostatic pressure : SAAG > 1.1

= Portal hypertension with its causes :

- Liver cirrhosis : The most common cause.
- Supra-hepatic causes :
 - RSHF, constrictive pericarditis, TI & TS
 - Budd- Chiari syndrome & IVC obstruction.
- Infra-hepatic causes : Portal vein thrombosis.

b) Diminished osmotic pressure (Hypoalbuminemia) :

- End stage liver disease : poor protein synthesis.
- Nephrotic syndrome.
- Nutritional : severe malnutrition , malabsorption.

c) Miscellaneous:

- Meig's syndrome: (ovarian tumor, Ascites & pleural effusion)
- Myxedema : does not cause ascites directly. The ascites occurs because of myxedema related congestive heart failure.
- Chronic hemodialysis : occurs in fluid overloaded dialysis , most of patients also have cirrhosis.

II. Exudative ascites : $\uparrow$ permeability of peritoneal capillaries, SAAG < 1.1

- Peritoneal disease : TB peritonitis , SBP. - Mesothelioma.
- Pancreatitis.

III. Chylous ascites : Thoracic duct obstruction (by lymphoma).

Clinical picture:**Symptoms:**

- **D**istension.
- **D**yspepsia.
- **D**yspnea.
- **D**evelopment of abdominal hernia.

Signs:**1- Inspection:**

- **D**istension of the abdomen (mainly in flanks) $\pm$ visible vein.
- **D**iverticulation of recti.
- **D**ownward shifted , everted umbilicus and may be umbilical hernia.
- **D**ilated veins on the abdominal wall :
 - Portal hypertension : Caput medusa.
 - IVC obstruction.

2- Palpation:

- Fluid thrill in tense ascites.
- Liver & spleen may be felt by dipping method in tense ascites.
- Abdominal masses may be felt : in TB & malignancy.

3- Percussion:

- Rounded central resonance with a peripheral “ U ” shaped dullness in the flanks down to the bed. The resonance over the umbilicus occurs in ascites because bowel floats on the top of abdominal fluid.
- **Shifting dullness** in moderate ascites (> 500 ml) : It is the most important clinical sign of ascites.
- Percussion in Knee elbow position in mild ascites (< 500 ml) : dullness around the umbilicus.

4- Auscultation:

- Venous hum may be heard over dilated vein.
- Puddle sign (auscultatory percussion) : see clinical book

Pleural effusion may occur secondary to ascites : due to passage of fluid through defects in the diaphragm.

Differential diagnosis :

F's (causes of abdominal distension)

- F**at (obesity) : sunken umbilicus , no shifting dullness.
- F**luid (ascites) : flanks > centre (*frog abdomen*).
- F**ull urinary bladder : umbilicus shifted upward , fullness is central.
- F**latus (gaseous distension) : generalized hyper-resonance.
- F**etus (pregnancy) : needless to say in ♀ only . ☺

Investigations:

I. Investigations to detect the ascites :

Abdominal ultrasound & CT : detect ascites even in very small amount (30 ml) & also detect the cause e.g. liver cirrhosis.

II. Ascetic fluid analysis : To detect the type of ascites

- **Serum-Ascites Albumin Gradient (SAAG)** : see below
- Cell count :
 - An ascetic fluid with high RBCs suggests :
 - Malignancy.
 - TB.
 - Pancreatitis.
 - An ascetic fluid with high WBCs :
 - PMN > 250 /mm³ ⇒ suggests SBP.
 - TB peritonitis : > 70% lymphocytes.

- Culture & sensitivity test : Ziehl Neelsen stain (ZN) for TB.
- Amylase to exclude pancreatic ascites.
- Cytology for malignant cells.

	Exudate	Transudate	
- Proteins	>	<	3 gm%
- Specific gravity	>	<	1016
- LDH	>	<	200 IU/L

III. Investigations for the cause :

- For liver cirrhosis : liver function tests , Ultrasound.
- For TB & malignancy : laparoscopy & biopsy.

Serum - Ascites Albumin Gradient (SAAG)

- It is calculated by :

Serum Albumin - Ascitic fluid Albumin concentration

MC

- Clinical value :

- **SAAG $\geq$ 1.1** $\Rightarrow$ *indicates that the ascites is due to portal hypertension regardless of its cause e.g. Liver cirrhosis, Congestive heart failure, Budd-Chiari syndrome.*
- **SAAG $\leq$ 1.1** $\Rightarrow$ Exudative ascites (*non portal hypertension etiology*) **e.g.**
 - Infection : TB , SBP.
 - Cancer : 1ry or metastasis.
 - Pancreatitis.
 - Vasculitis.
 - Nephrotic syndrome.

Treatment:

See before (6 items)

Refractory ascites :

- Ascites with lack of response to : 400 mg spironolactone plus 160 mg lasix daily with salt restricted diet for at least one week.
- Lack of response : Mean weight loss of less than 0.8 kg over 4 d and urinary sodium output less than the sodium intake.
- There are 2 types :
 1. Diuretic-resistant ascites : Lack of response to sodium restriction and diuretic treatment.
 2. Diuretic-intractable ascites : Development of diuretic-induced complications that prevent the use of an effective diuretic dosage.
- Diuretic-induced complications :
 - Hepatic encephalopathy.
 - Renal impairment.
 - Hyponatremia, Hypo- or hyperkalemia.
- Currently, serial large volume paracentesis (LVP), transjugular intrahepatic porto-systemic shunt (TIPS) & liver transplant are the mainstay treatment options.

Etiology	Treatment
Lack of salt resection	Treated by adequate salt restriction
Severe hypoalbuminemia	IV albumin.
Hyponatremia	Fluid restriction & IV manitol
Associated serious conditions : e.g. SBP (<i>spontaneous bacterial peritonitis</i>)	Treatment of the cause e.g. Cefotaxime: or Ciprofloxacin for 10 days.
Terminal case	• Le veen shunt : Peritoneo- venous shunt • TIPS. • Ascites ultrafiltration & reinfusion : Aspiration of ascetic fluid to concentrate it, then reinfusion to the patient IV. • Liver transplant.

Malignant ascites:**Etiology:**

- 1- 2ry tumor : Stomach, liver, pancreas.
- 2- 1ry tumors : Mesothelioma (rare).

Clinical picture:

- 1- **M**assive rapidly accumulating ascites.
- 2- Abdominal **m**asses.

Aspiration of Ascitic fluid:

- Hemorrhagic.
- **M**assive.
- **M**alignant cells.

Premature ascites:

Ascites in cirrhotic patient before shrunken liver e.g.

- Bleeding.
- Hepatitis.
- TB peritonitis.

- Ascites without LL edema:

- Ascites precox e.g. pericardial effusion.
- Local peritoneal disease.
- Diuretic therapy (e.g. *lasix*) in cirrhotic ascites may cause relieve of LL edema with persistence of ascites.

Causes of Hepatomegaly:

- 1- **Infections:** Hepatitis, Bilharziasis, Amoebiasis, Fascioliasis, TB.
- 2- **Inflammation:** Connective tissue disease & rheumatic disease.
- 3- **Infiltration:** Fatty liver, glycogen storage disease & amyloidosis.
- 4- **Malignancy:** 1ry & 2ry, Leukemia, Lymphoma.
- 5- **Congestive** liver.
- 6- **Cholestasis:** obstructive Jaundice particularly extra-hepatic.

- Mild enlargement: < 5cm from costal margin.
- Moderate enlargement → 5-8 cm from C. margin.
- Severe enlargement > 8cm below C. margin e.g. Leukemia, Lymphoma, Amyloidosis.

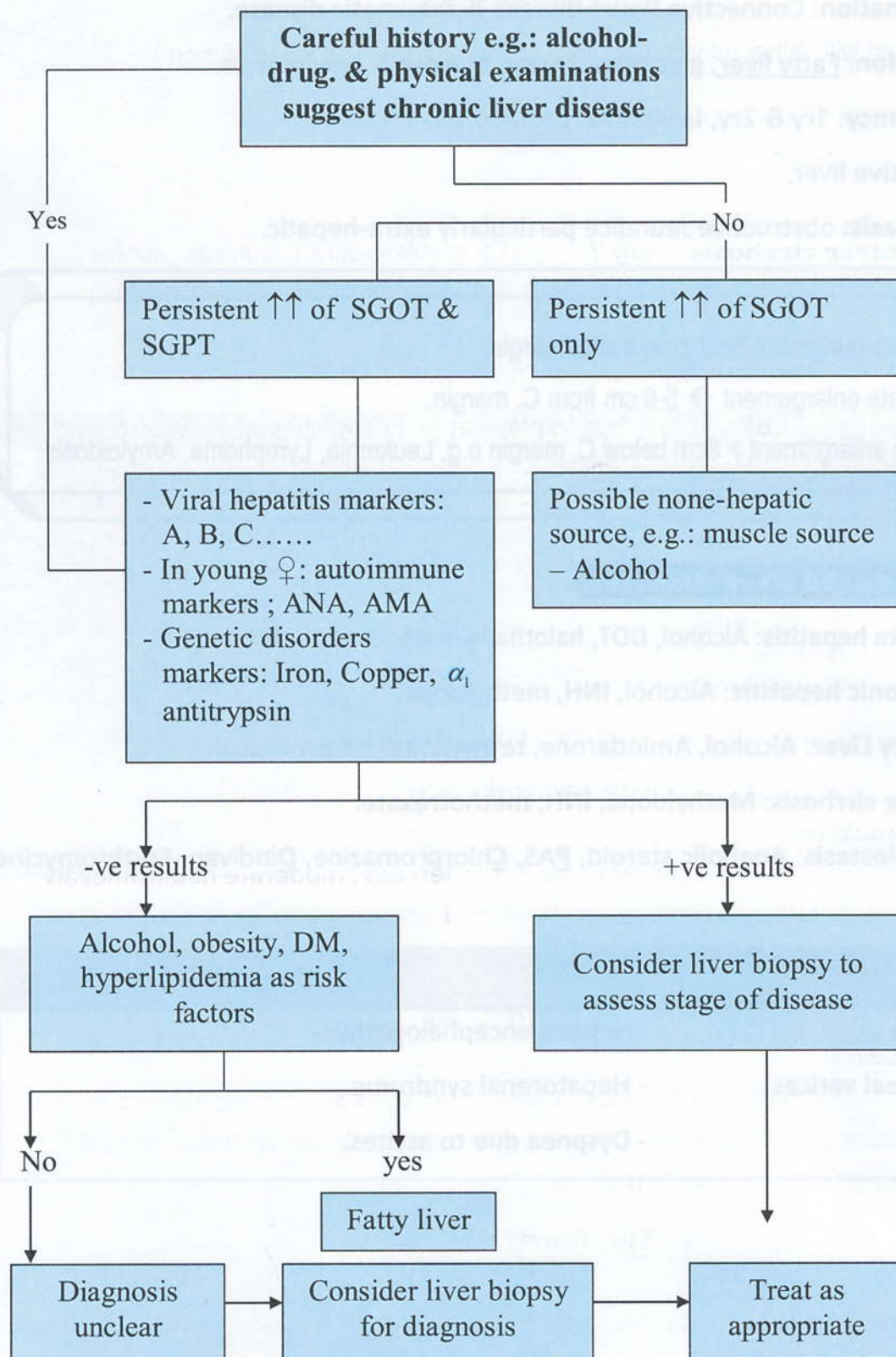
Drug induced liver diseases:

- 1- **Acute hepatitis:** Alcohol, DDT, halothane, paracetamol, INH.
- 2- **Chronic hepatitis:** Alcohol, INH, methyldopa.
- 3- **Fatty Liver:** Alcohol, Amiodarone, tetracycline, valproic acid.
- 4- **Liver cirrhosis:** Methyldopa, INH, methotrexate.
- 5- **Cholestasis:** Anabolic steroid, PAS, Chlorpromazine, Dindivan, Erythromycine.

Hepatic emergencies:

- | | |
|----------------------|---------------------------|
| -FHF | - Hepatic encephalopathy. |
| -Esophageal varices. | - Hepatorenal syndrome. |
| -Fever. | - Dyspnea due to ascites. |

Approach to asymptomatic patient with elevated transaminases :



Liver commentaries

The first case

The case start with either Bilharziasis (farmer) or hepatitis (blood transfusion)



Liver cirrhosis

why ?

☞ LCF manifestations (Jaundice , ascites , ...)

☞ Portal hypertensions (Esoph. varices)



Complicated by : one of the following 5

Hepatoma	SBP	Hypersplenism	Encephalopathy	B.corpulmonale
- Rapid unexplained deterioration. - Resistant ascites. - Paramalignant syndrome.	- Aspiration of ascetic fluid : WBCs > 250/cm² - Improved by antibiotics. - Resistant ascites. - Abdominal tenderness & fever.	- ↓ WBCs, RBCs, platelets - Notice that portal hypertension is an important cause of hypersplenism.	- Precoma manifestations (2 SAD) - Coma.	- History of B. - pulmonary HTN. - RSHF

So,.. the final diagnosis is liver cirrhosis complicated by one of the 5's above.

The second case

Ameobic hepatitis :

A case of fever , right upper quadrant pain & tenderness , moderate hepatomegaly with or without jaundice , ↓ air entry on base of right lung (e.g. pleural effusion) . Also leucocytosis , ↑↑ alkaline phosphatase.

The third case

Wilson disease :

The family history, clinical examination & laboratory tests show the presence of acute liver failure, plus neurological manifestations e.g. abnormal movement. All point to the diagnosis of Wilson's disease.

The fourth case

Acute hepatitis

Jaundice, right upper quadrant pain, fatigue and markedly elevated ALT & AST make the diagnosis of acute hepatitis.

1- A 42 year old man presented because of increasing abdominal girth over the previous 2 weeks. His weight had increased only 3 pounds . He denied recent fever , chills, nausea , vomiting , melena , hematemesis or abdominal pain ,but did have a previous episode of esophageal variceal bleeding treated with sclerotherapy.

Physical examination :

Temp. 37C , pulse : 84b/m , Respiratory rate : 20/m , BP : 110/70 mmHg .

General : chronically ill appearing , Eyes : sclera icterus , skin : spider angiomata .

Abdomen : distension , venous redistribution pattern on the abdominal wall, tense ascites , bowel sounds present . Liver not palpable and splenic tip palpable . Edema lower limbs.

Lab finding : WBC 11.400/cmm , with 87% PMNs , Het 31% , platelets 85000/cmm, PT 11.5 seconds , Na 137mEq/L , K 5.2mEq/L , HCO_3^- : 27 mEq/L , AST : 72 , ALT : 58 IU/L , Alkaline phosphatase : 18 KAU , Total serum bilirubin : 2.8 mg/dl , Paracentesis : ascites fluid is cloudy with WBC 1050/cmm , with 56% PMNs , ascites fluid protein 3 gm/dl . serum albumin 2.5 gm/dl . Medication including spirinolacton , frusemide , but a good response after addition of antibiotic.

- a) What is the professional diagnosis ?
- b) Mention causes of hematemesis ?
- c) What are causes of portal hypertension ?
- d) What are the pathogenesis of the ascites in hepatic patient ?
- e) In this patient, What is the most probable cause of ascites ?
- f) What is the most suitable antibiotic used in treatment ?

a) What is the professional diagnosis ?

Liver cirrhosis complicated by Spontaneous Bacterial Peritonitis (SBP).

- Cirrhotic patients with ascites and evidence of any clinical deterioration should undergo diagnostic paracentesis to exclude SBP.
- SBP occurs in 10% of cirrhotic patient due to loss of detoxification function of the liver. The key to the diagnosis of SBP is examination of the ascetic fluid : Neutrophils count > 250 cells / mm^3 .

b) Mention causes of hematemesis ?

See GIT book

c) What are causes of portal hypertension ?

See GIT book

d) What are the pathogenesis of the ascites in hepatic patient ?

See GIT book

e) In this patient, What is the most probable cause of ascites ?

Spontaneous bacterial peritonitis

f) What is the most suitable antibiotic used in treatment ?

Cefotaxime: 2 gm t.d.s...IV or Ciprofloxacin 400 mg/12h for 5 - 10 days.

2- A 35 year old farmer , while working in the field , felt dizziness , fainting , extreme fatigability , nausea ,sweating and collapse . He was transferred to hospital where he passed black motion . On examination there was marked pallor , pulse 110/minute , BP : 90/60 mmHg . Abdominal examination revealed moderate enlargement of spleen. He was managed and discharged well in few days.

- a)** Mention 5 data from the history that could help in reaching the diagnosis ?
- b)** Mention 5 added signs to clarify the diagnosis ?
- c)** What is the most probable diagnosis ?
- d)** Mention investigations that could be of help in assessing the case ?
- e)** How could you treat such case ?

a) Mention 5 data from the history that could help in reaching the diagnosis ?

- 1- Farmer.
- 2- Splenomegaly.
- 3- Melena (black motion)
- 4- ↑ pulse.
- 5- History of drug intake , bleeding from other orifices , Dyspepsia.

b) Mention 5 added signs to clarify the diagnosis ?

- 1- Signs of portal hypertension : Splenomegaly, Caput medusa.
- 2- Signs of ascites : see GIT book P 70
- 3- Liver cirrhosis.
- 4- Spider naevi , palmer erythema , pallor , jaundice.
- 5- PR : to exclude hemorrhoids , fissure.
- 6- Signs of RV enlargement.

c) What is the most probable diagnosis ?

Complicated portal hypertension (Rupture esophageal varices)

DD :

- Causes of upper GIT bleeding :
- B polyposis.
- B corpulmonale : syncope

3- HCV antibody positive patient is concerned that he may transmit the virus to his wife or children. They are tested and are to be negative for HCV antibody.

He is relieved but asks for advice to prevent infecting them.

a) What do you advise him ?

b) Enumerate extra-hepatic manifestations of hepatitis C ?

- a)**
- HCV is spread by parenteral contact with infected blood. In contrast to hepatitis B , sexual transmission of HCV is inefficient thus, it is NOT recommended that couples in long term relationship alter their sexual practices (e.g. use of condoms, etc ..)
 - Hepatitis C is NOT spread by hugging, sneezing or sharing a drinking glass.
 - Household members of persons infected with HCV should not share items that might be contaminated with small amount of blood , such as nail clippers

4- A 14 year old boy presented with yellowish discoloration of the sclera, he gave a history of tiredness and fatigue for the previous few weeks. His mother gave a family history of similar presentation few years ago in his older sister and she died few weeks later.

On examination : The boy was conscious & afebrile but jaundiced. Pulse 100/m, BP 110/70. Chest and heart were clinically free. Abdominal examination showed shifting dullness. Bilateral mild lower limb edema was present. There were abnormal movements involving both upper limbs.

Investigations : total bilirubin 3.5 mg/dL, direct bilirubin 2.8 mg/dL, albumin 3 g/dL, AST 556 U/L, ALT 678 U/L, INR 2.5

- a) What is the most likely diagnosis ?
- b) What further investigations should be done ?
- c) What is the treatment of this condition ?

a) The most likely diagnosis is **Wilson's disease**. The family history, clinical examination & laboratory tests show the presence of acute liver failure , plus abnormal movement. All point to the diagnosis of Wilson's disease.

b) Further investigations :

- Serum ceruloplasmin (low) and urinary Cu excretion (should be elevated).
- Slit lamp examination of the cornea for the presence of Kayser Fleischer ring.
- Brain MRI.
- Liver biopsy.

c) Treatment :

- Cu chelation : D penicillamine.
- Supportive measures for acute liver failure.
- Liver transplantation.

5- A 32 year old male went for a pre-employment assessment. He had past history of blood transfusion once 10 years ago after a car accident. Examination revealed no clinically detectable abnormalities. Investigations ALT 120 U/L, AST 80 U/L , total bilirubin 1 mg/dL, Anti-HCV- Ab positive.

- a) What further investigations would you recommend ? And why ?
- b) What are the drugs used in treatment of this condition ? What is the duration of treatment ?
- c) What are the contraindications of treatment ?

a) The investigations :

I. Lab :

- Serum albumin, PT, CBC to assess the presence of liver cirrhosis.
- PCR : Hepatitis C virus RNA to confirm the diagnosis. Anti HCV Ab by ELISA is used only for screening.

II. Imaging :

- Abdominal US : to assess the presence or absence of cirrhosis, portal HTN, Size of spleen.

III. Liver biopsy is indicated to detect the chronic hepatitis activity and degree of fibrosis.

b)

- Combined ttt with pegylated interferon & ribavirin is used in the ttt of chronic HCV
- Dose , Precautions : see book
- Duration of ttt : for 12 months. Treatment should continue for longer period especially in a case of HCV genotype 4 (genotype in Egypt).

c)

- Decompensated cirrhosis is considered a contraindication.
- Renal failure is an absolutely contraindication for ribavirin.

6- A 17 year old male presented to the outpatient clinic with fever, anorexia, and vomiting. The condition started 4 days before, and was associated with right hypochondrial pain that was not related to meals. There was no change in bowel habits. He noticed tea colored urine for the last day . There were no previous medical illness or drug intake.

Examination revealed temp 38 C, pulse 120/m, normal BP. He was jaundiced. Abdominal examination revealed tenderness over the right hypochondrium, hepatomegaly 5 cm below the costal margin. There was no Splenomegaly or ascites.

Investigations : Serum ALT 2650 U/L, AST 2320 U/L, total bilirubin 5 mg/dL, indirect bilirubin 2.2 mg/dL.

a) What would be the possible diagnosis ? And Why ?

b) What further tests would you recommend to confirm the diagnosis ?

c) What is the treatment ?

a) The diagnosis is an acute hepatitis (most probably Hep A)

- Jaundice, right upper quadrant pain, fatigue and markedly elevated ALT & AST make the diagnosis of acute hepatitis.
- The age, the absence of drug history plus the typical symptoms and signs make the diagnosis of hepatitis A most appropriate.

b) Anti HAV Ab (IgM) should be recommended to confirm the diagnosis.

c) Treatment is conservative (bed rest & symptomatic ttt). The condition is benign, resolves gradually and NOT complicated by chronicity.

Malabsorption Syndrome

Definition:

- Failure of absorption of one or more of the nutrient (fat, proteins, CHO, minerals ...)
- **Steatorrhea** (fatty stool) remains the main mark of malabsorption.

Causes:

4

I- Gastric Causes:

4

- 1-Gastrectomy.
- 2-Atrophic gastritis.
- 3-Cancer stomach → achlorhydria ($\downarrow$ HCl)→Bacterial Contamination of intestine.
- 4-Zollinger-Ellison's syndrome → hyperchlorhydria ($\uparrow$ HCl) → inhibits pancreatic lipase.

II- Hepato-biliary Causes :

4

- 1- Liver Cirrhosis
- 2- Chronic hepatitis.
- 3- Biliary obstruction.
- 4- Biliary fistula.

III- Pancreatic Causes :

4

- 1- Chronic pancreatitis
- 2- Cystic fibrosis
- 3- Cancer head of pancreas.
- 4- Pancreatectomy.

IV- Intestinal Causes :

(The most common)

A) Primary causes:

- 1- Tropical sprue: unknown etiology but may be:
 - Bacterial, viral , parasitic infection.
 - Folic acid deficiency.
- 2- Coeliac disease: (Non-tropical sprue , Gluten sensitive enteropathy)
 - Autoimmune disorder in which there is an abnormal reaction to gluten (protein found in wheat) → Ag. Ab reaction → damage of intestinal mucosa.
 - C/P : severe malabsorption syndrome , associated autoimmune diseases.
 - Complications : small intestine carcinoma , $\uparrow$ incidence of lymphoma.
 - Investigations : Jejunal biopsy → villous atrophy , IgA antigliadin antibodies
 - Treatment : The only effective treatment is lifelong gluten free diet.

B) Secodary to intestinal diseases:

- 1- **Short gut syndrome**: extensive intestinal resection → ↓ absorptive surface.
- 2- **Stagnant (blind) loop syndrome**: Stagnation of intestinal content e.g. strictures of small intestine, Diverticulosis → **bacterial overgrowth** → mucosal injury & nutrients utilization.
- 3- **Systemic diseases**: DM, amyloidosis, hypothyroidism, CHF.
- 4- **Infection**: -Bacterial over growth.
-TB enteritis, Giardia, Strongeloides.
- 5- **Inflammation**: Crohn's disease, Irradiation.
- 6- **Iatrogenic**: **A**ntacids, **B**iguanides, **C**holestyramine, **D**endivan.
- 7- **Lymphatic obstruction**:
 - Lymphoma.
 - Whipple's disease : (mainly affects MAN)
Malabsorption Syndrome, Arthritis, Neuropathy & lymphadenopathy.

Clinical picture:

4

I. General manifestations:

- 1- Loss of weight.
- 2- Fatigue.
- 3- Fever
- 4- Clubbing of fingers.

II. Intestinal manifestations:

- 1- **Steatorrhea**: Stool is Pale, bulky, offensive, floats on water, greasy, glistening.
- 2- **Diarrhea**: malabsorption usually results in diarrhea.
- 3- Audible intestinal sounds (*borborygmi*).
- 4- Distension, colic.

III. Nutritional deficiency:

- protein → muscle wasting, edema, recurrent infections
- Fat → loss of weight.
- CHO → hypoglycemia.

- Minerals:
 - Iron → anemia.
 - Na → Muscle cramps, hypotension.
 - K → arrhythmia.
 - Ca, Mg → tetany.
 - Iodine → Goitre.
- Vitamins:
 - A → night blindness, follicular hyperkeratosis.
 - D → Rickets, osteomalacia.
 - E → infertility.
 - K → Bleeding tendency.
 - C → Scurvy
 - B1 → Beri – Beri.
 - B2 → glossitis – gastritis.
 - B3 → Diarrhea, Dermatitis, Dementia.
 - B6 → peripheral neuritis.
 - B12 → Megaloblastic anemia.

IV. **C/P of the cause:** Coeliac disease , history of surgical operation

Investigation: 4

I- Biochemical investigation: 4

- 1- Estimation of fecal fat: (n : 6 gm/d)
 - in steatorrhea → total fat is increased (> 6 gm/d)
 - split fat → intestinal disease ▪ Non split fat → pancreatic disease
- 2- Pancreatic function tests.
- 3- Sugar curve : flat curve.
- 4- **D-xylose test:**

25 gm D xylose (*poorly metabolized sugar*) is given orally then collect urine over the next 5 hours.

 - Normally : 5 hours urine should contain at least 5 gm *provided that normal renal functions.*
 - In malabsorption syndrome : 5 hours will contain less than 5 gm

II- Hematological Investigations : 4

- 1- **Blood picture:** Anemia. (Microcytic anemia due to iron deficiency or macrocytic anemia due to vitamin B₁₂ or Folate malabsorption.
- 2- **Plasma proteins :** hypoproteinemia.
- 3- **Serum electrolytes.**
- 4- **Prothrombin time:** may prolonged because of malabsorption of vitamin K.

III- Radiological investigations: 4

- 1- CT 2- MRI 3- U.S.
- 4- Barium meals:
 - ◇ Dilatation of intestinal lumen. ◇ Loss of normal feathery appearance.

IV- Investigations for bacterial overgrowth :**1) 14 C- Xylose breath test :**

- ↪ 14 C-Xylose is given orally then measure the 14 CO₂ in the breath.
- ↪ In bacterial overgrowth : ↑ 14 CO₂ in the breath because more bacteria will act on 14 C- Xylose.

2) Aspiration of jejunal content then culture.**Treatment:**

- 1- Treatment of the cause:
 - T.B enteritis : anti TB drugs.
 - Tropical sprue : antibiotic (tetracycline) & folic acid.
 - Coeliac disease :
 - The only effective treatment is lifelong gluten free diet.
 - Cortisone.
- 2- Diet: Low fat, low fibers, non irritant diet.
- 3- Parenteral vitamins, minerals, fluid.
- 4- Symptomatic treatment :
 - e.g. Anti diarrheal drugs : Difenoxylate (*Lomotil*) , Loperamide (*Loperazin*).

Diarrhea

Definition:

It means an increase of stool liquidity , quantity (> 200g/d) or frequency (N: 4 motions/d).

Etiology:

I- **Etiology of acute diarrhea:** *Acute onset with < 2 weeks of symptoms.*

Acute diarrhea is generally infectious and self limited.

1- Infection:

- **Bacterial** : Salmonella , Shigella , E.coli , Cholera, Campylobacter.
- **Viral** : Rota virus , Norwalk virus.
- **Protozoa**: E.histolytica , Malaria , Giardiasis
- **Helminthes**: Ascaris , strongyloids stercoralis.

MCQ

- ➡ Organisms that cause bloody diarrhea include : Salmonella, Shigella, E.coli, Campylobacter.
- ➡ Diarrhea after ingestion of raw eggs or dairy : think Salmonella.
- ➡ Campylobacter is the most common etiology of infectious diarrhea.

2- Iatrogenic :

- ✎ Laxatives.
- ✎ Antibiotic.
- ✎ Chemotherapy.
- ✎ Parasympathetics.
- ✎ Mg hydroxide.
- ✎ Allopurinol.

- **Mg** hydroxide → diarrhea (**M**ust **g**o to the bathroom)
- **Aluminum** hydroxide → constipation (**A**lu**m**inum amount of feces)

3- Toxins :

- Bacterial: staph, E.coli
- Lead
- Arsenic

4- **Diet**: Unripe fruit, Alcohol, Mushroom, food allergy.

5- **Nervous**: psychological stress e.g. before *internal medicine* exam. ☹

II. **Etiology of chronic diarrhea:** *Gradual onset with > 4 weeks of symptoms.*

1- **Malabsorption syndrome.** (enumerate *its causes*)

2- Diseases of the colon :

- Irritable bowel syndrome.
- Inflammatory bowel diseases e.g. ulcerative colitis.
- Cancer colon.

3- Endocrinal causes :

- Thyrotoxicosis.
- Diabetic neuropathy.
- Addison's disease.
- Zollinger Ellison syndrome.
- Carcinoid tumor.

Mechanisms of Diarrhea:

i. **Osmotic (Malabsorption)diarrhea:**

Presence of non absorbed , hypertonic substances in intestinal lumen maintain fluid & prevent absorption (e.g. lactulose, sorbitol, magnesium).

ii. **Secretory diarrhea** (*watery diarrhea*) :

↑↑ secretion of water & electrolytes into the lumen.

e.g. cholera , E.coli , ↑ VIPs (*vaso - active intestinal peptides*)

iii. **Abnormality of intestinal motility** : e.g. Thyrotoxicosis, IBS, D neuropathy.

iv. **Abnormality of intestinal mucosa** : e.g. inflammation (IBD)

Causes of bloody diarrhea :

- Bacterial : Campylobacter, shigella, salmonella, TB, E coli, clostridium difficile.
- Parasitic : Amebiasis, bilharziasis.
- Ischemic colitis (inadequate blood supply)
- Radiation colitis.

Complications :

- $\downarrow$ $H_2O \rightarrow$ dehydration.
- $\downarrow$ $K \rightarrow$ hypokalemia.
- $\downarrow$ $HCO_3 \rightarrow$ Acidosis with normal AG

Diagnosis:

how to reach diagnosis of a case of diarrhea?

1- History analysis:

- **Frequency:** $>4/d \rightarrow$ diarrhea
 - If the stool is of large volume & not excessive frequent $\rightarrow$ small bowel disease.
 - If the stool is of small volume & excessive frequent $\rightarrow$ large bowel disease.
- **Consistency:**
 - Watery: inflammation
 - Greasy: malabsorption.

2- Examination:

- Abdominal tenderness
- Bowel sounds
- Degree of general hydration
- Examination per rectum: to exclude rectal mass or blood.

3- Investigations: 4 S

- *Not every patient who presents with diarrhea needs to be evaluated with these expensive tests, watchful waiting & symptomatic therapy with oral fluid are very enough.*
- *Acute diarrhea usually does not require laboratory investigation unless the patient has a high fever, bloody diarrhea or diarrhea lasting > 5 days.*
- **Stool examination :**
 - For ova, cysts & parasites. - Fat assay.
 - Stool osmolarity (osmotic gap)

Osmotic gap = Stool osmolality - 290 (N : < 50 mOsm/kg)

More than 50 = presence of more osmotically solutes in stools e.g. lactulose.

- **Sigmoidoscopy** : if a large bowel cause is suspected.
- **Small bowel radiology** : if a small bowel cause is suspected.
- **Serological tests.**

Plus

- **Investigations Of malabsorption syndrome** : (see before).

Treatment : 3 S

- **Specific** : treatment of the cause.
- **Symptomatic**:
 - Anti diarrhea : Diphenoxylate (*lomotil*) , Loperamide (*loperazine*)
 - Anti emetic: Motilium.
- **Supportive**:
 - Diet: ↓ fat, ↓ irritants , light diet.
 - Treatment of complications: Fluid – K – HCO_3 .

Algorithm for diagnosis of chronic diarrhea :**Exclude :**

1. Causes of acute diarrhea.
2. Lactose intolerance.
3. Previous gastric or ileal surgery.
4. Parasitic infections.
5. Medications.
6. Systemic diseases.

1. Fecal leucocytes & occult blood.
2. Sigmoidoscopy with biopsy.
3. Upper GI endoscopy & barium enema.

Abnormal

IBD Cancer

Normal

Stool electrolytes, osmolality,
weight/24h, quantitative fat.

Increased osmotic gap**Normal osmotic gap****Increased fecal fat****Normal fecal fat****Increased stool weight****Normal stool weight**

- Malabsorption syndrome
- Pancreatic insufficiency.
- Bacterial overgrowth.

- Lactose intolerance*
- Laxative abuse.
- Lactulose

> 1000 g
Secretory diarrhea.

Irritable bowel syndrome.

Current medical Diagnosis & Treatment, 48th ed. 2009

***Lactose intolerance :**

- Result from a deficiency of lactase enzyme that hydrolyzes the disaccharide lactose into glucose and galactose.
- C/P : abdominal bloating, flatulence, watery diarrhea following milk ingestion.
- Treatment : Avoidance of dairy products, Lactase enzyme replacement.

DIYSENTERY

Definition :

Diarrhea + Tenesmus + Blood + mucous in stool.

Tenesmus : painful defecation with sense of incomplete bowel evacuation.

Etiology :

- Amoebic dysentery
- Bacillary dysentery, Bilharzial dysentery.
- Cancer colon, rectum.
- Diverticulosis.
- Malaria
- Renal failure
- Giardia (v. rare).

Dysentery Scheme :

- Causative organism :
- Mode of infection :
- C/P : * Asymptomatic * Symptomatic * Complications
- Investigations : 4 S
- Treatment : 3 S

Amoebic dysentery

- **Causative organism** : E. histolytica (cyst form)
- **Mode of infection** : feco-oral
(ingestion of cysts which resist gastric acidity → transformed into vegetative form in the intestine & then passes to the colon)
- **Clinical picture** :
 - 1- **Asymptomatic** : just cysts in the stool.
 - 2- **Symptomatic** :
 - a. Acute.
 - b. chronic

a. **Acute Amoebic dysentery :**- **Symptom:** *One word***dysentery :** (mild diarrhea (8/d) , Tenesmus , blood & mucous in stool)- **Signs:**○ **Local :** Tenderness in colon especially caecum & sigmoid.○ **General :** - **No** fever (*superficial lesion*)- **No** dehydration (*mild diarrhea*)b. **Chronic Amoebic dysentery :**

- Recurrent attacks of acute dysentery alternating with normal bowel habits.

- Abdominal pain may occur (over the caecum , appendix , transverse colon).

3- **Complications:**○ Local: Amoeboma (*mass in the right iliac fossa*)○ Systemic: Amoebic hepatitis (*see hepatology*).**Investigations:** 4S- **S**tool examination: cysts , mucous , blood.- **S**igmoidoscopy: flask shaped ulcer with intervening healthy mucosa.- **S**mall bowel radiology- **S**erological tests : antibodies may be detected in the serum of the patient**Treatment :** 3 S- **S**pecific : *anti amoebic*- **S**ymptomatic- **S**upportive} **Like diarrhea****Antiamoebic drugs:**

4 , 3 , 2

I- **Luminal amoebicidal :** used for treatment of cysts (*chronic amoeba*)1- Halogenated quinoline e.g. *di-Iodo-hydroxy quinoline*

- SE: Neuropathy, goiter - Dose: 500 mg t.d.s for 2 weeks.

2- Phenanthroline quinines (*Entobex*) : 500 mg t.d.s for 2 weeks.3- Diloxanide (Furamide) : 500 mg t.d.s for 1 week4- Antibiotic: paromomycin & erythromycin are directly amoebicidal.

II- Systemic drugs: (*Acute & extra intestinal Manifestation*)

Have no effect on cyst in intestinal lumen

- 1- Emetine: SE: Cardiotoxicity
- 2- Dehydro-emetine: less toxic
- 3- Chloroquine: used in hepatic amoebiasis.

III- Luminal & systemic (Mixed):**1- Metronidazole (Flagyl)**

- Dose: 750 mg t.d.s for 10 days - SE: nausea, metallic taste.

2- Tinidazole: (fasigyn) : 2 gm daily for 5 days**Bacillary dysentery**

Causative organism: G-ve bacilli (shigella)

Mode of infection: feaco-oral.

Clinical picture :

Asymptomatic

Symptomatic:

➤ **1st phase** (1-2 days) : fever – colic – diarrhea.

➤ **2nd phase** (1-2 weeks) :

○ **Dysentery** :

(severe watery diarrhea (15 /d), tenesmus , mucous & blood in stool)

○ **Abdominal pain** & tenderness.

○ **General signs:** fever, malaise , dehydration.

Complication:

Can't see .. Can't pee, Can't climb the tree ♪ ♪

Urethritis – Arthritis – Conjunctivitis. (**Reiter's syndrome**).

Investigation: 4S

- **Stool examination:** Excess WBCs & RBCs , Culture: shigella
- **Sigmoidoscopy:** diffuse inflammation with dirty yellowish pseudomembrane.
- **Small bowel radiology.**
- **Serological test.**

Treatment : 3 S

➤ **Specific :**

- **Ciprofloxacin** : 500 mg twice daily for 5 days.
- Tetracycline: 2.5 gm in single oral dose.
- Septrin (Co. Trimexazole) : 2 tab twice daily for 5 days.

➤ **Symptomatic :**

- Anti spasmodic : for severe abdominal pain.
- Anti diarrheal drugs : are **better to be avoided** as they decrease the intestinal motility and hence decrease the wash of the organisms.

➤ **Supportive :** ↓ irritants , Excess fluids, vitamins.

Bilharzial dysentery

Causative organisms:

Mainly due to *S. mansoni* & very rare due to *S. hematobium*.

Mode of infection:

The parasite penetrates the skin during swimming in infected water.

Clinical picture: Incubation period : 2 months

Asymptomatic

Symptomatic:

- (1) **Dysentery** : → Severe diarrhea alternating with constipation.
→ Tenesmus
→ Mucous & blood in stool

(2) **Bleeding per rectum**

(3) **Pericolic tender mobile mass in left iliac fossa (bilharzioma)**

(4) **Hepato-splenomegaly (Egyptian splenomegaly) .**

Complications:

- **Hepatic bilharziasis. (.....)** see Hepatology
- **Bilharzial cor-pulmonale (.....)**

Investigations: 3S + 3 B

- **S**tool analysis: Bilharzial ova
- **S**igmoidoscopy: polyps or ulcers mainly in recto-sigmoid area.
- **S**erological test (by ELISA) : Schistosoma antibodies.
- **B**arium enema: polyps.
- **B**lood picture: Anemia – esinophilia.
- Investigations for **p**ortal hypertension.

Treatment:**i. Anti bilharzial drugs :** **Praziquantel** (*Biltracid*)

- Mechanism of action : Ca influx into the worm → marked contraction & spastic paralysis of the worm.
- Dose: 40mg / kg / once.
- S/E: headache, abdominal pain, nausea, vomiting, pruritis, fever, elevation of liver enzymes.

 Oxamniquine (*vansil*) : 20 mg/kg orally for 3 doses

- Against *S. mansoni* only.
- Safe in chronic hepatic forms of the disease, may cause fever.

 Niridazole (*ambilhar*) : 25 mg/kg/d orally for 7 days. **Metrifonate** (*Bilarcil*) : 10 mg/kg orally once every 2 weeks (repeated 3 times).

- Against *S. hematobium*.
- S/E : abdominal pain, nausea & vomiting.

 Mirazid (*Commiphora ext.*): Herbal drug , dose : 12 capsules over 6 days.

- Antibilharzial drugs must be given early before tissue fibrosis.
- Repeated courses may be needed as the worms migrate into the liver & return back to the periphery.
- Fever & vitamins deficiencies must be treated before starting therapy.

- ii. **Endoscopic polypectomy.**
- iii. **Treatment of the complications** e.g. Portal hypertension.
- iv. **Symptomatic & supportive treatment.**

VOMITING

Definition:

Forceful expulsion of gastric content into the mouth.

Mechanism of vomiting reflex:

→ stimulus → centre → response (vomiting)

- **Stimulus:**
 - peripheral (GIT).
 - Central e.g.: ↑ ICT.
 - Metabolic e.g.: uremia.
- **Centre :** vomiting centre in the medulla.
- **Response:** vomiting.
 - ◇ Pylorus is closed.
 - ◇ cardia is opened.
 - ◇ contraction of the diaphragm& abdominal wall muscles.

Etiology:

I- Peripheral causes: (GIT causes)

- Gastritis
- Peptic ulcer
- Cancer stomach
- Hepatitis
- Pancreatitis
- Appendicitis
- Cholecystitis
- peritonitis
- Pyloric or intestinal obstruction.

II- Central causes:

- Psychic : bad smell, sight.
- Anorexia nervosa.
- ↑ ICT: Tumor , Hemorrhage.
- Pain: migraine, MI, renal colic.

III- Metabolic causes:

- Renal failure.
- Liver cell failure.
- Acidosis (DKA).
- Electrolyte: ↑ Ca, ↓ Na, ↓ or ↑K

IV- Iatrogenic:

MAD

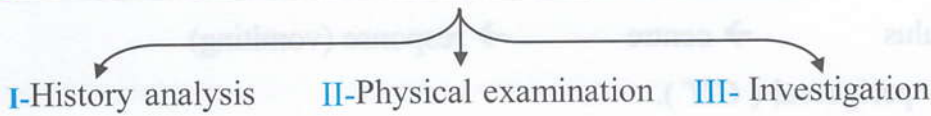
- morphine.
- Alcohol.
- Digitalis.

V- Pregnancy.

Complications of severe vomiting :

ABCD

- Alkalosis (tetany)
- Pulmonary aspiration.
- Cerebral hemorrhage.
- Dehydration.

Diagnosis of a case of vomiting:**I- History analysis :****(1) Time of vomiting:***** Early morning :**

- ☐ Pregnancy
- ☐ ↑ ICT
- ☐ Alcohol

*** During meal : Esophageal cause.***** After meal by:**

- ☐ ½ h : Gastric ulcer.
- ☐ 2-4 h : Duodenal ulcer.
- ☐ > 8h : Intestinal obstruction.

(2) Associated nausea: upper GIT causes.

- No nausea: ↑ ICT

(3) Associated Abdominal Pain : (GIT causes)

- e.g. peritonitis , intestinal obstruction , pancreatitis , cholecystitis
- Painless vomiting : Neurological causes.
- Pain relieved by vomiting : Gastric ulcer.

(4) Associated headache: ↑ ICT.**(5) History of drug intake :** MAD**(6) Biliary symptoms:**

Jaundice , Pruritis , Abdominal Pain , change of color of urine & stool.

(7) Frequency: Persistent in peritonitis.

II- Examination of vomiting:

- **Amount** : huge in pyloric obstruction .
- **Color** : coffee ground as in hematemesis.
- **Content** :
 - Undigested food: pyloric obstruction.
 - Bile: below ampulla of Vater
 - Blood: ulcer, cancer, Mallory weiss \$
 - F.B. : gall stone.
- **Odour**: offensive as in intestinal obstruction , malignancy.

III- Investigations: investigations for the causes.**Treatment :**

- **Specific**: for the cause.
- **Symptomatic**:
 - ✎ Antiemetic : motilum , primpran.
 - ✎ Antidiarrheal drugs.
- **Supportive** : correct dehydration & electrolyte imbalance.

CONSTIPATION

Definition:

Presence of 2 or more of the following :

- Hard stool.
- Infrequent stool < 3/week.
- Incomplete evacuation.
- Straining is more than 25% of the time of defecation.

Causes:

8 I

- i. **I**mmobility (prolonged rest in bed).
- ii. **↓** Intake of fluid & fibers.
- iii. **I**gnoring urge.
- iv. **I**rritable bowel syndrome.
- v. **↓** Intestinal motility : hypothyroidism , DM , $\uparrow$ Ca , $\downarrow$ K, DM, scleroderma.
- vi. **I**atrogenic: codeine , morphine , anticholinergic, aluminum hydroxide, iron.
- vii. **I**nflammation : ulcerative colitis , diverticulitis .
- viii. **I**ntestinal obstruction : cancer colon , stricture, anal fissure.

Approach to a case of constipation :

I. History : Dietary history & fluid intake, medications & associated symptoms.

II. Examination :

- Manifestations of the cause.
- PR examination : to identify fissures, hemorrhoids which may be caused by constipation.

III. Investigations :

- Investigations for the cause : e.g. Serum Ca, glucose, Thyroid function tests, ..
- Colonoscopy : especially in patients over 50 years with anemia, weight loss, bleeding per rectum, positive occult blood test, or family history of cancer colon.

Treatment :

- I. Treatment of the cause : medical or surgical.
- II. General :
 - Reassurance.
 - Diet : increase fluid & fiber intake.
- III.Laxative :
 - Bulk laxative : fiber based laxative.
 - Osmotic laxative : lactulose.
 - Stimulant laxative : senna.
 - Softener laxative : mineral oil.

INFLAMMATORY BOWEL DISEASE

(Crohn's disease & ulcerative colitis)

Etiology:

- Is still questionable.
- Most probably autoimmune. (The local T cells are angry with something in the food)
- Genetic factor: play a great role.
- Infections (T.B, measles): not confirmed.
- Psychological factor may play a role.

	Crohn's disease	Ulcerative colitis
Pathology: - Site: - Layers - Granuloma - Crypt abscesses - Fibrosis	- Affects any part of GIT, particularly the <u>ileocecal region</u> in a <u>discontinuous pattern</u> (<i>Skip lesions</i>). - The rectum is often spared. All three (<i>transmural</i>) Yes in (30%) No N.B: finding of granuloma = crohn's disease Severe	- The <u>rectum</u> is always involved, & extend proximally to the <u>colon</u> in a <u>continuous pattern</u>. - Terminal ileum can be affected in 5% only - Mucosa & submucosa only No Yes (30%) N.B: finding of crypt abscesses = ulcerative colitis No
C/P: - Sex - Age - Smoking - Abdominal Pain:	Equal No specific age ↑↑ incidence in smokers Prominent	Slightly more in ♀ ☺ 30-40 Y ↓↓ incidence in smokers (80% non smokers) Less prominent

	Crohn's disease	Ulcerative colitis
- Diarrhea	Yes	Yes <i>(severe & sometimes dysentery)</i>
- Bleeding per rectum	Uncommon	Common
- Anal & oral lesions	Yes	No
- Bowel obstruction	May be	No
-Malabsorption S.	May be	No
- Intestinal fistula	May be	No
- B ₁₂ deficiency	May be	No
- Carcinoma risk	Minor	High. Significant risk 2-3 decades after onset.
- Toxic megacolon : It is a condition in which the colon becomes atonic & dilated. More common in ulcerative colitis.	Rare	○ Worsening of the patient clinical condition and development of fever, tachycardia & leukocytosis. ○ Treatment : antibiotics & prompt surgical consultation

- Extra intestinal manifestations : 🖐

• Skeletal :

- Peripheral arthritis.
- Sero -ve spondylopathy e.g. Ankylosing spondylitis : in 30% of patients with IBD.
- Osteoporosis : secondary to the disease process itself, & the medications commonly used for treatment (e.g. corticosteroids).



• Skin : 🎵 🎵

- Erythema nodosa : painful, red, subcutaneous nodules.

Treatment:

Medical treatment : 4 "S"s ☺

- 1- **Sulfasalazine**: reduce inflammation especially in ulcerative colitis.
1 gm /6 h reduced to a maintenance dose of 2 gm/ day for 2 years after remission .
- 2- **Steroid** (prednisone) : 60mg/d. This is the main treatment for active disease
- 3- Immuno **Suppressants**: **Azathioprine** (*Imuran*).
- 4- **Symptomatic** :
 - Antibiotics for 2ry infection : Metronidazole & ciprofloxacin.
 - Prebiotics, Probiotics.
 - Anti diarrheal drugs.

Surgical treatment : (Indications)

- Failure of medical treatment.
- Severe complications



: Dr. Ahmed Mowafy
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IRRITABLE BOWEL SYNDROME (IBS)

Definition:

It's a functional disturbance of colonic motility with no organic cause.

Etiology :

Unknown , psychological disturbance play a role.

Clinical picture:

long history with long free interval

- Recurrent pain :over any part of the colon (especially in left iliac fossa).
- The pain is ↑↑ by food & ↓↓ by defecation.
- There is constipation or diarrhea.
- Abdominal distension is common.
- Patient with IBS often complain of anxiety , depression & tension headache.

Investigations :

(to exclude common diagnosis)

- No +ve finding.
- IBS is a diagnosis of exclusion.

Treatment :

- ☺ Reassurance.
- ☺ Diet : high fiber diet & bran , Avoid coffee , tea , smoking.
- ☺ Mild sedative , antispasmodics, antidiarrheals (*Loperamide*).
- ☺ Tegaserod (*Zelmac*) : *one tablet / 12 h*

It activates serotonin type 4 receptors in GIT.

DYSPEPSIA

Definition:

Any abdominal discomfort related to meal e.g. heartburn, epigastric pain, distension, nausea, vomiting

Causes of dyspepsia :

- **GIT causes :** - Peptic ulcer. - Reflux esophagitis - Cholecystitis
- Pancreatic disorders - Hepatic diseases.
- **Systemic diseases :** Renal failure, hypercalcemia, DM.
- **Drugs :** NSAIDs, cortisone, digitalis.
- **Functional dyspepsia :** it's a persistent dyspepsia with no organic cause
(-ve endoscopy & the patient is Helicobacter pylori – negative).

Diagnosis :

History analysis:

- What type of discomfort does the patient feel ? e.g. heartburn, distension...
- Is this discomfort related to meal ?
- Time to meal :
 - **During meal :** Esophageal cause : Reflux esophagitis.
 - **½ H after meal :** Gastric cause e.g. Peptic ulcer .
 - **2-3 H after meal :** Duodenal cause e.g. Duodenal ulcer.
 - **8 H after meal :** Intestinal cause : obstruction .
- Type of meal :
 - ☺ Fat : Cholecystitis ☺ Meat : Cancer stomach . ☺ Starch : Gastric ulcer .
- Associated symptoms.

Investigations :

for the cause

Patients with persistent dyspepsia need to be referred for **endoscopy** if they are **over 50 years old**, or they have associated weight loss, dysphagia, GIT bleeding or previous gastric surgery.

Treatment :

- ☺ **Diet :** eat little & often, Avoid fatty food, tea, coffee, smoking, alcohol.
- ☺ **Symptomatic treatment.**
- ☺ **Treatment of the cause.**

Diseases of Esophagus

- The esophagus is 25 cm long connecting the pharynx to the stomach .
- The mucosa is lined with squamous epithelium .
- The esophagus is protected from acid damage by a number of defenses including the lower esophageal sphincter pressure , gravity ,salivary bicarbonate & esophageal bicarbonate secretion .

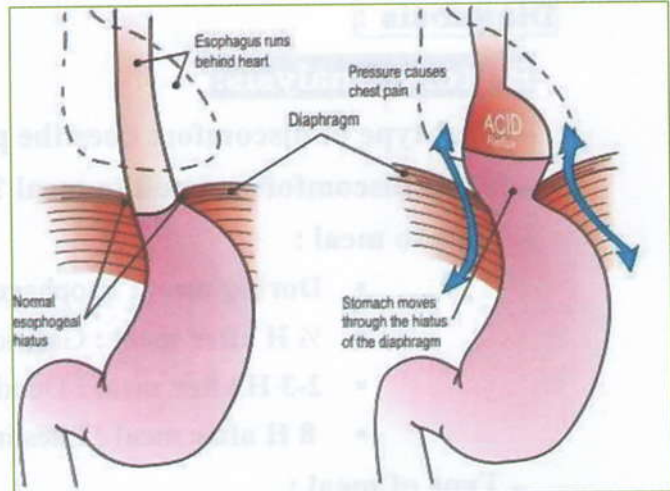
Hiatus Hernia

- Occurs when part of the upper stomach herniates through the diaphragm into the chest.
- It's extremely common , especially with increasing age & obesity .
- **There are 2 types :**

1. Sliding type.
2. Rolling type.

1- Sliding 80 % :

- May be asymptomatic.
- Acid reflux & aspiration.
- Bleeding may occur.
- **Investigations :**
 - Barium swallow.
 - Endoscopy.
- **Treatment :**
 - Weight reduction (Meals should be small)
 - Sleeping in semi-sitting position .
 - H2 blockers & proton pump inhibitors (*omeprazole*)
 - Prokinetic drug : domperidone (*motilium*) .
 - **Surgery :** indicated in resistant cases (*fundoplication*)



2- Rolling 20 % : (para-esophageal hernia)

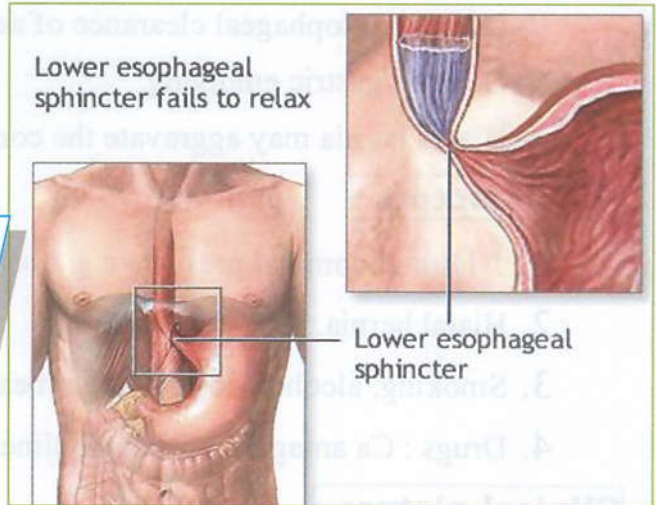
- Here , a small part of the fundus of the stomach rolls up alongside the esophagus through the hiatus .
- The gastro-esophageal junction is not affected so , there is no reflux
- may obstruct or strangulate .
- A big hernia may lead to mediastinal syndrome .
- Surgery is indicated in severe cases.

Esophageal Achalasia

Definition :

It's a motor disorder of the esophagus characterized by **impaired relaxation of the lower esophageal sphincter (LES)** and loss of peristalsis in the distal two-thirds of the esophagus.

The musculature of the upper $\frac{1}{3}$ of the esophagus is skeletal, whereas that of the lower $\frac{2}{3}$ is smooth muscle.



Clinical picture :

- Progressive dysphagia.
- Regurgitation , chest pain , infection , weight loss & nocturnal cough may occur.

Investigation :

1. Barium swallow:

- Esophageal dilatation with a **bird's beak tapering** of the distal esophagus.
- Absence of gases in the fundus of the stomach.

2. Upper endoscopy .

- #### 3. Manometry :
- High pressure in lower segment,
Loss of peristalsis.



Treatment :

- Nitrates, CCBs or endoscopic injection of botulinum toxin (*Botox ingestions*) into the LES may provide short term relief of symptoms.
- Ballom dilatation or surgical (Heller®) myotomy are options of choice. Endoscopic dilatation or surgical myotomy .

GASTRO-ESOPHAGEAL REFLUX DISEASE

(GERD)

Definition : Reflux of gastric contents into the esophagus.

Etiology & pathogenesis : (Failure of anti reflux mechanisms)

- 1- Decrease tone of lower esophageal sphincter (LES) .
- 2- Decrease esophageal clearance of acid due to poor esophageal peristalsis.
- 3- Delayed gastric emptying.
- 4- Hiatus hernia may aggravate the condition.

Risk factors : 4

1. ↑ intra-abdominal pressure e.g. obesity, pregnancy.
2. Hiatal hernia.
3. Smoking, alcohol, coffee, large meals (especially late at night).
4. Drugs : Ca antagonist , theophylline , anticholinergic & nitrates.

Clinical picture : 4

1. **Heartburn** : The main symptom, 30 - 90 min after a meal, Increased on lying down & relieved by antacid, sitting or standing. Retrosternal chest pain can be difficult to distinguish from other causes e.g. angina. ☹
2. Pulmonary manifestations : Asthma, pneumonitis, pulmonary fibrosis.
3. Laryngeal irritation : chronic cough, morning hoarseness may occur.
4. Exam is usually normal unless a systemic disease e.g. scleroderma is present.

Complications : 4

1. Erosive esophagitis causing upper GIT bleeding.
2. Aspiration of gastric contents (aspiration pneumonia).
3. Peptic stricture causing dysphagia.
4. **Barrett's esophagus** : (May occur in long standing acid reflux) .
 - The normal squamous epithelium is replaced by the columnar gastric epithelium.
 - It's a premalignant leading to adenocarcinoma.

BARRett's esophagus :

Esophagus **B**ecomes **A**denocarcinoma **R**esult from **R**eflux ☺☺

Investigations: (GERD is a clinical diagnosis) 4

1. Esophageal PH monitoring (gold standard for diagnosis) .
2. Endoscopy.
3. Manometry.
4. Barium swallow : it may show hiatus hernia .

Treatment : 4

1- Diet :

- Limit intake of food & drink that reduce lower esophageal sphincter pressure e.g. Fatty food , acidic foods, onions ,chocolate, coffee, alcohol .
- Avoid heavy meals especially before sleep.
- Weight reduction.
- Stop smoking.

2- Postural therapy :

- Raising the head of the bed at night .
- Avoid lying down after eating .
- Remain upright at least 2h after eating .

3- Drug therapy :

a) ↓ gastric acidity :

- ✎ Proton pump inhibitors : Omeprazole , most potent single agent.
- ✎ Antacid.
- ✎ H₂ blockers : Ranitidine.

b) ↑ esophageal peristalsis : Domperidone (*motilium*)

4- Surgical & Endoscopic therapy : In resistant cases.

DYSPHAGIA

Definition:

Difficulty of swallowing (*dysphagia*) or pain with swallowing (*odynophagia*) due to abnormalities of the oropharynx or esophagus.

Causes :

1- Transfer dysphagia : " neurological causes "

(alteration of neuromotor mechanism of the oropharyngeal phase)

- Bulbar palsy.
- Myasthenia gravis, myopathies & polymyositis.
- Stroke.
- Motor neurone disease.

2- Transit dysphagia : (Functional , abnormal peristalsis)

- Achalasia .
- Scleroderma .
- Esophageal spasm.

3-Obstructive dysphagia: (mechanical narrowing of the esophagus)

- Esophageal stricture.
- Esophageal webs : Plummer Vinson syndrome.
- Cancer esophagus.
- All causes of mediastinal syndrome : Goitre , bronchogenic carcinoma , LN

4- Odynophagia : (painful swallowing)

- Inflammation of (mouth, tongue, pharynx, tonsils or esophagus)

5- Hysterical : (Globus hystericus)

Diagnosis of a case of dysphagia :

History analysis : Ask about :

- Onset , Course , Duration.
- Type of food (solid or liquid)
- Painless or painful.
- Associated symptoms .
- Site of obstruction .

Examples :

Transfer dysphagia :

- ♥ **Onset** : Acute
- ♥ **Course** : variable .
- ♥ **Type of food** : more to **liquid** .
- ♥ **Associated symptoms**: Nasal regurgitation, Dysphonia, neurological manifestations.

Transit dysphagia :

e.g. **Achalasia**

- ♥ Intermittent & may progress –long duration.
- ♥ **Liquid** > solid.
- ♥ Relieved by repeated swallowing.
- ♥ **Associated symptoms** : Heartburn precipitated by eating , no marked loss of weight .

e.g. **Scleroderma**

- ♥ Intermittent course .
- ♥ Both solids & liquids .
- ♥ Associated symptoms : Nocturnal cough , regurgitation .

NB : Dysphagia that worsens on ingestion cold liquids & improves with warm liquids suggests a motor disorder(transit dysphagia).

Obstructive dysphagia :

Cancer esophagus

- ♥ Progressive – short duration .
- ♥ Dysphagia to **solids** that may progress to include liquids.
- ♥ Associated symptoms : weight loss , chest & back pain.

Esophageal webs :

Associated with iron deficiency anemia & glossitis (*Plummer-Vinson syndrome*)

Investigations :

- **Barium swallow** followed by endoscopy, manometry and/or pH monitoring.
- If an obstructive lesion is suspected, proceed directly to endoscopy with biopsy.

MESENTERIC ISCHEMIA

↓ mesenteric blood supply leading to insufficient perfusion to intestinal tissue and ischemic injury.

Etiology :

1. Acute arterial occlusion :
 - Thrombosis (due to atherosclerosis).
 - Embolism (due to AF).
2. Nonocclusive arterial disease : Low cardiac output., Arteriolar vasospasm.
3. Venous thrombosis : hypercoagulable disease.

Clinical picture :

- Sudden onset of severe abdominal pain.
- History of similar abdominal pain after eating (*intestinal angina*) may be present.
- Nausea, vomiting, diarrhea & bloody stool.
- Early examination is often unremarkable, later finding may include peritoneal signs (suggest bowel infarction).

Complications :

- Sepsis, MOF & death. *The mortality rate for acute mesenteric ischemia is > 50%.*

Investigations :

1. Lab tests : leukocytosis, metabolic acidosis with ↑ lactate, amylase & LDH.
2. X ray & CT : bowel wall edema.
3. Mesenteric **angiography** : is the gold standard for arterial occlusive disease.

Treatment :

1. Volume resuscitation.
2. Antibiotics (broad spectrum)
3. Anticoagulation : for arterial or venous thrombosis or embolism.
4. Thrombectomy & endovascular stenting for acute arterial thrombosis.
5. Resection of infarcted bowel.

Stomach & duodenum

Physiological aspect :

- HCL is secreted by the parietal cells of the stomach through the action of hydrogen-Potassium ATPase (proton pump)
- **Function of HCL :**
 - Converting pepsinogen to pepsin , initiating the first stages of protein digestion.
 - Antibacterial barrier.
- **HCL secretion is stimulated by :**
 - Vagus (directly & via increasing gastrin)
 - Gastrin.
 - Histamine.
- **HCL secretion is inhibited by :** **MCQ**
 - Somatostatin ▪ Secretin ▪ Cholecystokinin

N.B.

- Parietal cells → secrete HCL & intrinsic factor.
- Peptic cells (chief) → secrete Pepsin.
- G cells → secrete Gastrin.

Peptic ulcer

Definition :

- Ulceration of mucosa which is exposed to acid peptic juice.
- The following sites are affected :
 - Duodenum.
 - Stomach.
 - Jejunum (after gastrojejunostomy)
 - Esophagus.
 - Meckel's diverticulum (contains ectopic gastric tissue)

Etiology :

- It occurs when stomach acid penetrates the stomach and/or duodenal lining.
- **It's a mix of :**
 - Hyperacidity : duodenal ulcer.
 - Decreased mucosal resistance : gastric ulcer.

1- **Helicobacter pylori infection** (duodenal > gastric)

2- **Traditional NSIDs :** (gastric > duodenal).

3- Rare causes : Zollinger Ellison syndrome (gastrin-producing tumor)

- **S**moking , **S**picy , **S**tress are no longer thought to be a cause of ulcers , but they can make ulcers worse (*aggravating factors*)
- Smoking → ↑ acid & ↓ protective prostaglandin.

1- **Helicobacter pylori :**

- Responsible for the majority of peptic ulcer (90% of DU , 70% of GU).
- H.pylori is a gram -ve spiral bacillus transmitted by feco-oral or through mouth to mouth such as kissing.
- Many people have H.pylori infection, but not everyone who has an infection will develop a peptic ulcer.
- Pathogenesis of H.pylori :
 - ↓ somatostatin.
 - ↑ gastrin release.
 - Produce cytotoxins causing mucosal inflammation.

2- Non steroidal anti-inflammatory drugs (NSAIDs) :

- NSAIDs act by inhibiting cyclo-oxygenase enzyme (COX) leading to decrease prostaglandin → mucosal erosions & ulceration.
- Notice that prostaglandin play a big role in gastric protection.

NB : All people at high risk of developing peptic ulcer should use COX-2 inhibitor rather than one of the traditional NSAIDs (COX-1 inhibitor) , however studies have shown that COX-2 inhibitors appear to increase the risk of heart attacks & stroke with long term use , so most doctors now use a traditional NSAIDs plus a strong acid inhibitor.

Disorder associated with peptic ulcer :

- **C**irrhosis.
- **C**RF.
- **C**OPD.
- **C**oronary diseases.

NB : Peptic ulcer is more common in cirrhotics due to ↓ destruction of gastrin & histamine by the liver & ↓ mucosal resistance due to congestive gastropathy caused by portal hypertension.

Clinical picture :

Symptom : Epigastric pain

- Character :

- Classically presents with chronic or periodic dull burning epigastric pain.
- Sudden onset of severe generalized pain may indicate perforation.

- **Duration :** variable from few minutes to several hours.

- Relation to meal :

- DU : improves with meals, worsens 2 - 3 h after meals.
- GU : precipitated by food ½ h after meals

So, in DU : pain awakes the patient from sleep (*the most important symptom*)

After a meal, pain from a **G**astric ulcer is **G**reater, whereas **D**uodenal pain **D**ecreases. 😊

- Relieving factors :

- DU : antacid or food , so appetite ↑ (patient eats frequently to relief pain)
- GU : fasting , vomiting (some patients learn to induce vomiting for pain relief)

- Associated symptoms : Nausea , Hematemesis.**Signs :** may be -ve

- **Localized tenderness** at the site of ulcer (**severe tender suggests a perforation**).
- An acute perforation may present with a rigid abdomen, tenderness or other signs of peritoneal irritation.

Complications :

- GIT **bleeding** : most common complication (15%) , may be the first symptom.
- **Perforation** : The second most common complication.
- **Pyloric obstruction**.

Investigations :**1- Endoscopy with biopsy :** The best to detect the ulcer.

- *Endoscopic biopsy should be taken in all gastric ulcer to differentiate between benign & malignant ulcer. Malignant gastric ulcer is mostly malignant from the start.*

2- CBC to assess for GIT bleeding.**3- Occult blood** in stool.**4- Investigations for H. Pylori :****a. Non invasive :**

- Serological ELISA :

Positive serological tests don't necessarily mean active infection.

After treatment, antibody levels decline to undetectable levels in 50% of cases by 12-18 months.

- A fecal antigen immunoassay :

A positive test is indicative of active infection.

– **The 14C urea breath test :** MCQ

- The patient ingests urea labelled with 14C, then CO₂ produced by urease enzyme is detected in the exhaled breath.
- A positive test is indicative of active infection.

b. **Endoscopy with biopsy :**

- **Urease test :** H. pylori secrete a urease enzyme which splits urea to release ammonia. A biopsy sample is put into a jelly containing urea and a PH indicator; this will thus change color if H.pylori is present.
- Histological assessment.

5- In recurrent or refractory cases, serum gastrin may be used to screen for Zollinger-Ellison syndrome.

Treatment :

i. **Diet :**

- Frequent small meals.
- Avoid spicy food , smoking , alcohol.

ii. **Medical treatment :**

There are 3 categories :

- I. Acid anti-secretory agents.
- II. Mucosal protective agents.
- III. H. pylori eradication.

1. **Antacid:** (*symptomatic relief in mild cases*)

e.g. mixture of Aluminum & Mg hydroxide (*Maalox*)

2. **H₂ blockers:** (for 4-8 weeks)

They block H₂ receptors → reduction of acid secretion.

- ✎ Cimetidine : 200 mg four times/d . SE : reversible gynecomastia & impotence.
- ✎ **Ranitidine** (*Zantac*) : 150 mg twice /d or better 300 mg at bed time.
- ✎ Famotidine : 20 - 40 mg/d.

3. Proton pump inhibitors (PPI) : (for 4 - 6 weeks)

- They inhibit H - K ATPase enzyme (proton pump) $\rightarrow$ $\downarrow$ H^+ secretion $\rightarrow$ $\downarrow$ HCL secretion.

☒ Omeprazole (*Losec*) : 20 mg / d.

☒ Lansoprazole : 30 mg / d.

☒ Pantoprazole : 40 mg / d.

4. Sucralfate: (for 4 -6 weeks)

- It's a mucosal protective agent (*coating agent*)

- Dose : 1 gm / qid.

- Not given with antacid.

5. Prostaglandin analog : (Misoprostol)

- It is used for mucosal protection.

- *Misoprostol* can help patients with peptic ulcer who require NSAID therapy (e.g. for arthritis).

MCQ

6. Eradication of H. Pylori: (*triple therapy for 2 weeks*)

- No single agent is effective in eradication this organism.

- Triple therapy is used for 2 weeks e.g.

☒ Omeprazole 20 mg twice daily.

☒ Clarithromycin (*Klacid*) 500 mg twice daily.

☒ Metronidazole 500 mg/d or Amoxycilline 1 gm /d twice daily.

- Eradication of H. Pylori may lead to dramatic decrease in ulcer recurrence to less than 5%.

7. Avoid NSAIDs:

If NSAIDs must be continued , either use selective COX-2 inhibitors as Lomoxicam (*Xeфо*) or use traditional NSAIDs plus a strong acid inhibitor.

iii. Surgical treatment :

○ Indication :

- Refractory cases.
- Recurrent bleeding
- Perforation
- Pyloric obstruction.
- Malignancy.

○ Operations : Partial gastrectomy , Parietal cell vagotomy.

iv. **Treatment of complications :**

○ **Bleeding :**

- Ranitidine or Omeprazole infusion.
- Endoscopic injection of adrenaline.
- Blood transfusion.

○ **Perforation :** IV fluid , analgesic & antibiotic then surgery.

○ **Pyloric obstruction :** surgery.

Gall stones

Etiology :

1) Cholesterol stones :

Cholesterol is kept soluble by the presence of bile salts so, if bile salts decrease or cholesterol increases , cholesterol stones will occur.

2) Pigment stones : two

Excessive production of bile pigments in bile e.g. chronic hemolysis.

BM: gallstones are a mixture of cholesterol & bile pigment (mixed stones)

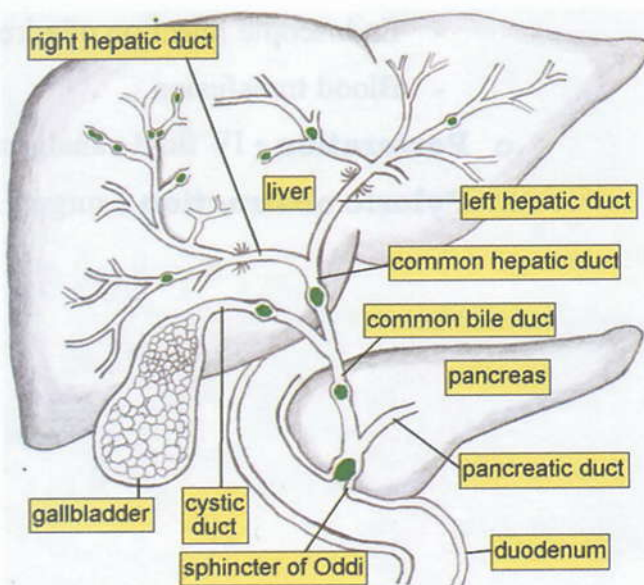
3) Strias :

○ Estrogen - due to GB wall relaxation.

Gall bladder & Biliary system

Anatomy of Biliary system :

- The right & left hepatic duct arise from the right & left lobes of the liver & unite to form the common hepatic duct which is joined by the cystic duct from the gall bladder to form the common bile duct (CBD) which enters the duodenum (*often after joining the main pancreatic duct*) through the ampulla of Vater.
- The **function** of the gall bladder is to store bile that is produced in the liver before the bile is secreted into the intestines.
- Approximately 1 litre of bile is secreted by the hepatocytes each day .Half of this drain directly into the duodenum & the remainder is stored in the gallbladder . Cholecystokinin then stimulates its release.



Gall stones

Etiology :

1) Cholesterol stones :

Cholesterol is kept soluble by the presence of bile salts so, if bile salts decrease or cholesterol increases , cholesterol stones will occur.

2) Pigment stones : rare

Excessive production of bile pigments in bile e.g. chronic hemolysis.

80% gallstones are a mixture of cholesterol & bile pigment (*mixed stones*)

3) Stasis :

- Estrogen : due to GB wall relaxation.

- Long term parenteral nutrition : lack of oral intake → ↓ cholecystokinin that stimulate the GB contraction.

Risk factors for stone formation :

- **F**atty (obesity) - **F**orty (increasing age)
- **F**ertile (multi parity) - **F**emale.
- **D**M - **D**rugs : contraceptive pills , Octreotide.

NB : *Stones may form in the CBD even after cholecystectomy.*

Clinical picture :

gall stones are present in 10 - 20% of population

- **A**symptomatic : 80% of cases.
- **A**bdominal pain : postprandial, usually in RUQ & radiates to right subscapular area, and is often associated with nausea & vomiting, & fatty food intolerance.
- **A**scending cholangitis (*bacterial infection*)
- **P**ancreatitis.
- **C**holecystitis.
- **O**bstructive jaundice if duct obstruction.

Investigations :

- **US :** should be performed routinely in patients suspected of having gallstones.
- **ERCP :** is the best technique for diagnosing common bile duct stones, but it is far less sensitive in detecting stones in the gallbladder than US.

The major component of most gallstones is cholesterol, which is not radio-opaque. This explains why many gallstones do not show up on a plain X-ray; only stones with high calcium content are radio-opaque and visible.



Treatment :

- **Cholecystectomy is a definitive treatment** (either surgical or by laparoscope)
- Medical treatment : through the oral administration of bile acids, such as *ursodeoxycholic acid* to dissolve cholesterol stones, with dietary modification (e.g. avoid fatty food).

Acute cholecystitis

Etiology & pathophysiology :

- It's usually caused by obstruction of the cystic duct by stones.
- Begins with sterile inflammation , then becomes infected (E.coli , Strept. fecalis)
- GB may distended with mucous (*catarrhal cholecystitis*) or pus (*suppurative cholecystitis*).
- Rarely, acute gangrenous cholecystitis may develop.

Symptoms : **Severe pain**

- This pain starts usually in the right upper quadrant or epigastrium.
- May radiate to the back or right shoulder.
- Biliary pain typically is gradual in onset and lasts hours.
- Nausea & vomiting may occur.

Signs :

- Fever is often present.
- Obstructive jaundice may occur due to edema or stone in CBD.
- **Murphy's sign** : Inspiratory arrest during deep palpation of the GB.
- **Boas's sign** :

There is an area of hyperesthesia between the 9th and 11th ribs posteriorly on the right side.

Investigations :**1- Laboratory :**

- Leucocytosis.
- Serum bilirubin , AST , ALT & alkaline phosphates : may be elevated.

2- Radiological : US , Radioisotope scanning.**3- ECG :** done as a routine especially in the elderly patients to exclude IHD.**Treatment :****Medical :**

- Bed rest , IV fluid.
- Analgesics : e.g. Pethidine.

No morphine as it induces spasm of the sphincter of Oddi.

- Antibiotic : 3rd generation cephalosporin.
- Antiemetic.

Surgical :

- Urgent surgery : in cases with complications.
- For stable patients or in patients with significant medical problems (e.g. DM) : delay cholecystectomy until acute inflammation resolves.(1-2 months)

Chronic Calculus Cholecystitis

Etiology :

It's almost always associated with the presence of gall stones.

Clinical picture :

- There are recurrent attacks of right upper abdominal pain.
- Dyspepsia , local tenderness & Murphy's sign is usually present.

Investigations :

US shows thick G.B. wall & gall stones.

Treatment :

Cholecystectomy.

Acute Pancreatitis

Etiology :

- gall stones → obstruction of pancreatic duct (*the most common cause*)
- Viral infection e.g. mumps, Coxsackie B.
- Alcohol.
- Hypercalcemia.
- Hyperlipidemia.
- Idiopathic.
- Iatrogenic : thiazide, post ERCP.

NB : Gall stones → back regurge of trypsin enzyme (*autodigestion*)

Symptoms :

- Abdominal Pain: epigastric pain radiating to the back.
- Nausea & vomiting.

- **Signs :** *Unexpectedly, abdominal signs are minimal in comparison with the severity of pain.*

- Tenderness & rigidity : at first in the upper abdomen, later on become generalized.
- **Cullen sign:** umbilical ecchymosis.
- **Grey turner's sign:** ecchymosis in flanks.

Complications:

- Multiple organ failure (MOF) : HF, Renal failure, Respiratory failure.
- Abscess.
- Pancreatic ascites.
- Hypo Calcemia.
- DIC.
- Diabetes mellitus.
- Obstructive jaundice : due to edema of the head of the pancreas.

Poor prognostic indicators :mnemonic : Pancreas

- **P**aO₂ < 60mmHg .
- **A**ge > 55 years.
- **N**eutrophils: WCC > 16,000 /mm³.
- **C**alcium < 8mg %.
- **R**enal: Urea > 100mg %.
- **E**nzymes: LDH > 350 ; SGOT > 250 U.
- **A**lbumin < 3gm%
- **S**ugar: Glucose > 200 mg % .

Investigation:

1. Pancreatic enzymes :

- Amylase (N : 75-150 somogyi unit) : ↑↑ (in blood , urine , peritoneal fluid)
- Lipase : ↑↑ , more specific than amylase.

NB : Serum amylase is raised in other conditions e.g. perforated peptic ulcer , ectopic pregnancy , alcoholics , salivary gland disease)

2. Peritoneal aspiration : contains high amylase.
3. Blood picture : leucocytosis , anemia in hemorrhagic pancreatitis.
4. X ray, US, CT : gall stones , swollen pancreas , calcification.
5. ECG : to exclude myocardial infarction.

Treatment :

- Nasogastric suction.
- Antibiotics.
- IV nutrition.

- Analgesics : pethidine (no morphine as it induces spasm of the sphincter of Oddi)
- Somatostatin infusion.
- Treatment of complications e.g. Respiratory support, cortisone.
- Surgery for pancreatic abscess & ERCP may be needed.

Prognosis :

- Roughly 85% are mild & self limited.
- 15% are severe, requiring ICU admission, mortality rate is about 50% of severe cases.

Chronic Pancreatitis

Chronic pancreatitis is an inflammatory condition characterized by irreversible damage to the exocrine & later to the endocrine tissue of the pancreas.

Etiology : Like Acute pancreatitis but :

- **Chronic alcoholism** is the commonest cause.
- Gall stones are unlikely to cause chronic pancreatitis.

Clinical picture : Triad of :

- i- Recurrent abdominal Pain: radiate to the back.
- ii- DM
- iii- Steatorrhea (*malabsorption*)

Investigation:

- Like acute pancreatitis.
- CT is the most sensitive for detection of pancreatic calcification.
- ERCP : shows irregular dilation and structuring of the pancreatic ducts.

Treatment :

1. Stop alcohol
2. Pancreatic enzyme replacement : taken as enteric coated tablets.
3. Symptomatic treatment :
 - pain : Analgesics.
 - Treatment of DM.
 - Treatment of steatorrhea.

Cancer Head of Pancreas

- Often asymptomatic, and thus presents late in the disease course.
- The classic presentation of pancreatic cancer is **painless progressive obstructive jaundice**.
- May present with abdominal pain radiating to the back.
- Obstructive jaundice.
- Anorexia, nausea, vomiting & weight loss.
- Examination : palpable, non-tender gall bladder (*Courvoisier's sign*).
- Investigation :
 - CT : to detect pancreatic mass, dilated bile ducts, the extent of vascular involvement.
 - US, ERCP.
- Treatment :
 - Unfortunately, most patients present with metastasis.
 - If no evidence of metastasis : resection using the Whipple procedure (*Pancreatico-duodenectomy*).
 - Chemotherapy with 5-FU & gemcitabine may improve short term survival, but long term prognosis is poor. (5% five year survival).

Cancer Body of Pancreas

- Pain: radiate to back.
- Jaundice: rare.

Tuberculous peritonitis

Etiology :

- **Primary :** Occurs in children by ingestion of infected milk (*bovine bacilli*)
- **Secondary :** Reactivation of a Tuberculous focus in the abdomen e.g. LN , Pulmonary TB.

Pathological type :

- 1- **Ascitic type :** Accumulation of free fluid in the peritoneum with no adhesion .
- 2- **Loculated type :** The peritoneal cavity is divided by fibrous adhesions into loculi containing ascetic fluid.
- 3- **Adhesive type :** Marked adhesion of the intestinal loops.

Clinical picture : usually gradual

Symptoms :

- General symptoms : night fever, night sweating, loss of appetite, loss of weight.
- Constipation or diarrhea (*malabsorption syndrome*).
- Abdominal pain & distension.

Signs : 2 T , 2 P

- **Toxemia :** toxic face , fever ,....
- **Tenderness** with mild rigidity.
- **Palpable masses** (rolled omentum)
- **Percussion** may reveal shifting dullness.

Complications :

- Intestinal obstruction.
- Intestinal fistula.
- Spread of tuberculosis.
- Amyloidosis.

Investigations :

- i. Abdominal Ultrasonography : detect mild ascites , LN.
- ii. X ray : calcified mesenteric LN.
- iii. Aspiration of ascetic fluid :
 - Straw colored.
 - Rich in lymphocytes & proteins.
 - Z.N. or PCR for the organism.
- iv. Laparoscopy or Laparotomy.

Treatment : Anti - Tuberculous drugs *see chest*

DD of epigastric pain :

Esophageal : - Esophageal spasm - Hiatus hernia. - Esophagitis. - Cancer.

Gastro-duodenal : - Gastritis - Peptic ulcer. - Gastric carcinoma.

Gall bladder : - cholecystitis. - Gall stones.

Pancreas : - pancreatitis. - Cancer pancreas.

Hepatic : - Hepatitis. - Congested liver. - Hepatoma.

Cardiovascular : -Angina - MI. - Pericarditis. - Aortic dissection.

Chest : -Pneumonia. -Pleurisy. - Repeated cough.

Nervous : - Herpes zoster. - Neurosis.

Medical conditions that mimic acute abdomen :

1. Myocardial infarction.
2. Rheumatic fever.
3. Dissecting aortic aneurysm.
4. Congestive heart failure : right upper abdominal pain due to congested liver.
5. Diabetic ketoacidosis.
6. Hypoglycemia.
7. Tetany.
8. Hyperparathyroidism.
9. Hemolytic crisis.
10. Henoch Schonlein purpura.
11. Acute intermittent porphria.
12. Acute pancreatitis.
13. Renal failure.
14. Familial Mediterranean fever. (*FMF*)
15. Vasculitis.
16. Irritable bowel syndrome (*IBS*).

Acute pain in the upper abdomen

Oesophagitis	<i>Suggested by:</i> retrosternal pain, heartburn.
	<i>Confirmed by:</i> oesophagogastroscopy.
Acute coronary syndrome (unstable angina or infarction)	<i>Suggested by:</i> chest tightness or pain on exertion.
	<i>Confirmed by:</i> exercise ECG, cardiac enzymes, coronary angiography.
Hiatus hernia	<i>Suggested by:</i> heartburn, worsens with stooping or lying, relieved by antacids.
	<i>Confirmed by:</i> oesophagogastroscopy, barium meal.
Gastritis	<i>Suggested by:</i> epigastric pain, dull or burning discomfort, nocturnal pain
	<i>Confirmed by:</i> oesophagogastroscopy, barium meal and pH study.
Gallstone colic (with no acute inflammation or infection)	<i>Suggested by:</i> jaundice, biliary colic, pain in epigastrium or right upper quadrant radiating to right lower scapula. No fever.
	<i>Confirmed by:</i> ultrasound of gallbladder and biliary ducts.
Acute cholecystitis	<i>Suggested by:</i> fever, guarding and positive Murphy's sign (abrupt stopping of inspiration when the palpating hand meets the inflamed gall bladder descending with the liver from behind the sub-costal margin on the right side, but not on the left side). ↑ WBC.
	<i>Confirmed by:</i> ultrasound gallbladder and biliary ducts.
Duodenal ulcer	<i>Suggested by:</i> epigastric pain, dull or burning discomfort, typically relieved by food, nocturnal pain.
	<i>Confirmed by:</i> oesophagogastroscopy, barium meal and pH study: (<i>Helicobacter pylori</i> often present in mucosa or serology).
Gastric ulcer	<i>Suggested by:</i> epigastric pain, dull or burning discomfort, typically exacerbated by food, nocturnal pain.
	<i>Confirmed by:</i> oesophagogastroscopy, barium meal and pH study.
Gastric carcinoma	<i>Suggested by:</i> marked anorexia, fullness, pain, large lymph node in the left supraclavicular fossa.
	<i>Confirmed by:</i> upper GI endoscopy with biopsy.
Pancreatitis	<i>Suggested by:</i> pain radiating straight through to the back, better on sitting up or leaning forward.
	<i>Confirmed by:</i> ↑ serum amylase, CT pancreas.

Acute central abdominal pain

Small bowel obstruction	<i>Suggested by:</i> vomiting, constipation with complete obstruction.
	<i>Confirmed by:</i> <i>X ray</i> shows small bowel loops and fluid levels.
Crohn's disease	<i>Suggested by:</i> chronic diarrhoea with abdominal pain, weight loss, palpable RLQ mass or fullness, mouth ulcers.
	<i>Confirmed by:</i> <i>colonoscopy with biopsy, barium studies</i> showing skip lesions.
Mesenteric artery occlusion	<i>Suggested by:</i> vomiting, bowel urgency, melaena, diarrhoea.
	<i>Confirmed by:</i> <i>mesenteric angiography, exploratory laparotomy.</i>
Abdominal aortic dissection	<i>Suggested by:</i> tearing pain , shock , hypotension and peripheral cyanosis.
	<i>Confirmed by:</i> <i>ultrasound or CT abdomen.</i>

Acute lateral abdominal pain

Pyelonephritis	<i>Suggested by:</i> pain in loin (upper lateral), rigors, fever, vomiting, frequency of micturition, renal angle tenderness.
	<i>Confirmed by:</i> <i>CBC: leucocytosis.urinalysis :</i> pyuria, urine culture and sensitivity
Renal calculus	<i>Suggested by:</i> renal colic mainly in loin (upper lateral), hematuria.
	<i>Confirmed by:</i> <i>urinalysis, renal ultrasound, IVU, CT/MRI.</i>
Ureteric calculus	<i>Suggested by:</i> renal colic, moving from loin (upper lateral) down to RLQ , hematuria.
	<i>Confirmed by:</i> <i>urinalysis, renal ultrasound, IVU, CT/MRI.</i>
Appendicitis	<i>Suggested by:</i> pain initially central, then radiating to <i>right</i> lower quadrant, anorexia, low grade fever, constipation. RLQ tenderness and guarding.
	<i>Confirmed by:</i> Inflamed appendix at laparotomy
Salpingitis	<i>Suggested by:</i> fever, nausea, vomiting, muco-purulent cervical discharge, irregular menses. Bilateral lower abdominal tenderness and guarding.
	<i>Confirmed by:</i> <i>CBC: leucocytosis. High vaginal swab, laparoscopy.</i>

Acute lower central (hypogastric) abdominal pain

Ulcerative colitis	<i>Suggested by:</i> abdominal pain, diarrhea with blood and mucus.
	<i>Confirmed by:</i> stool microscopy and culture, colonoscopy.
Large bowel obstruction	<i>Suggested by:</i> severe distension, late vomiting, visible peristalsis, resonant percussion, increased bowel sounds. Supine X ray showing peripheral abdominal large bowel shadow (with haustra partly crossing the lumen). Fluid levels on erect film.
	<i>Confirmed by:</i> abdominal ultrasound and laparotomy findings.
Cystitis	<i>Suggested by:</i> frequency, urgency, dysuria, hematuria. <i>Confirmed by:</i> urinalysis , culture & sensitivity test.
Ectopic pregnancy	<i>Suggested by:</i> constant unilateral pain , referred shoulder pain, amenorrhea , vaginal bleeding (usually less than normal period), faintness with an acute rupture.
	<i>Confirmed by:</i> pregnancy test +ve , bimanual examination reveals slightly enlarged uterus, pelvic ultrasound shows empty uterus.

Hepatology

I. SAQ (Short Answer Questions)

For cases, MCQ & oral exam

1- What is a major complication of ascites?

- Spontaneous bacterial peritonitis.
- Other complications : Abdominal hernia, renal failure, mesenteric venous thrombosis

2- What are the diagnostic criteria for SBP ?

Paracentesis : ascites fluid neutrophil count > 250 and positive culture or ascites fluid neutrophil count > 500

3- What is the most classic sign of SBP ?

Rebound abdominal tenderness in a patient with ascites.

4- As regard to hepatitis, what is window period? Which marker will be found in this period ?

Window period (gap) is the period between disappearance of HBsAg and appearance of HBsAb. During this period HBcAb IGM is always positive.

5- How many patients with hepatitis B virus infection develop chronicity?

It depends on route of transmission :

- Horizontal transmission : 10%
- Vertical transmission : 90%

6- What is vertical transmission of Hepatitis B ?

During labor admixture of maternal and fetal blood occurs. The virus is transmitted at the time of placental separation. So in a case of vaginal delivery, more chance of transmission. In HBsAg positive mother, manage baby with immunoglobulin + vaccine immediately after delivery.

7- Which hepatitis virus carries the highest risk of developing into hepatocellular carcinoma?

Hepatitis B

8- As regard to hepatitis B vaccination, what are the route of administration, time schedule and booster dose, duration of protection and Ab response after vaccination ?

- Route of administration : IM (deltoid)
- Time : 0, 1, 6 months and 5 years.
- Booster dose after 5 years in case of immunodeficiency, hemodialysis, persistent exposure.
- Duration of protection : about 10 years, may be lifelong.
- Ab response after vaccination : 1-3 months after 3rd dose
 - Ab < 10 IU/L : nonresponder
 - Ab 10-100 IU/L : low responder, booster dose should be given
 - Ab > 100 IU/L : high responder

9- Which hepatitis viruses cause acute viral hepatitis?

- Hepatitis A
- Hepatitis B ± Hepatitis D
- Hepatitis E

10- Does hepatitis C virus cause acute hepatitis ? Very rare.

11- Mention the percentage of post exposure risk following needlestick injuries.

Mnemonic : ACB

- ☠ AIDS : 3 in 1000 (0.3%)
- ☠ Hep C : 3 in 100 (3%)
- ☠ Hep B : 3 in 10 (30%)

- Post exposure management for Hep C : Serial determination of anti-HCV antibodies is recommended for 6 months.
- Post exposure management for Hep B :
 - Vaccinated : no need for treatment. Just reassurance.
 - Not vaccinated : IM injection of HB Ig & vaccination.

12- How can you detect an acute hepatitis A infection? HAV IgM

13- How can you detect immunity to hepatitis A? HAV IgG

- 14 What laboratory tests should be ordered to screen for acute hepatitis B infection?** HBsAg and IgM anti-HBc
- 15- What are the metabolic complications of fulminant hepatic failure ?**
- 16- What are the King's College Hospital criteria in a case of paracetamol toxicity?**
- 17- How much ascites fluid is necessary to detect clinically?**
It depends on the contour of the body. Usually 1L but may be 2L if obese.
- 18- What is the type of ascites in liver cirrhosis?**
Transudative ascites (SAAG > 1.1)
- 19- What is the treatment for SBP?**
3rd generation cephalosporin with albumin
- 20- What is ascending cholangitis ?**
 - Bacterial infection of the biliary tract secondary to obstruction.
 - E coli is the most common organism.
- 21- What are the classic symptoms of ascending cholangitis?**
Charcot triad : Jaundice, fever, RUQ tenderness
- 22- What are the lab finding consistent with ascending cholangitis?**
↑ WBCs, ↑ alkaline phosphatase, ↑ direct bilirubin, ↑ ALT
- 23- How is ascending cholangitis diagnosed?**
ERCP, PTC
- 24- What is primary sclerosing cholangitis?**
Chronic inflammation and fibrosis of biliary tree
- 25- Treatment of hepatitis C**
- 26- What is the organism of amebic liver abscess? And how does it enter into the liver?** Entamoeba histolytica enters liver through portal vein.
- 27- In which lobe of liver, abscess is more common and why?**
Abscess is more common in right lobe because of prominent right portal vein and its left branch is angulated at its origin.

28- What are the common presentations of amebic liver abscess?

Fever and right hypochondrial pain

29- What are the causes of hepatorenal syndrome?**30- Extrahepatic causes of cholestasis****Malignant :**

- Cholangiocarcinoma
- Pancreatic cancer
- Ampullary cancer
- Porta-hepatis LN malignancy

Benign :

- Choledocholithiasis
- Post-operative biliary structures
- Chronic pancreatitis

31- Intrahepatic causes of cholestasis

- Viral hepatitis : Hep A, B, C, D, E & Epstein-Barr virus
- Drug toxicity :
 - Pure cholestasis : anabolic steroids, contraceptive pills
 - Cholestatic hepatitis & chronic cholestasis : chlorpromazine
- Primary biliary cholangitis
- Primary sclerosing cholangitis
- Cholestasis of pregnancy
- Post operative cholestasis.

32- Mandatory criteria for diagnosis of primary biliary cholangitis

- Clinical (e.g. fatigue, pruritus, Xanthomas) & lab evidence of cholestasis e.g. serum alkaline phosphatase > 1.5 times of upper limit of normal
- AMA antibodies & elevated IgM
- Destructive cholangitis on liver biopsy.

33- What are the differential diagnoses of hepatic encephalopathy?

- Intracranial lesions : stroke, tumor.
- Infections : meningitis, encephalitis, and intracranial abscess
- Metabolic encephalopathy, such as hypoglycemia, hyponatremia
- Hyperammonemia from other causes e.g. secondary to ureterosigmoidostomy
- Toxic encephalopathy from alcohol intoxication.
- Toxic encephalopathy from drugs such as antidepressants, antipsychotic agents.
- Post seizure encephalopathy.

Gastroenterology MCQ

1- A 56 - year - old man presents to his internist with jaundice The patient is receiving no medication , and his only symptomatic complaint is mild fatigue over the past 2 months. Physical examination is remarkable only for the presence of sclera icterus. The patient has no significant past medical history. Analysis of serum chemistry reveals the following : SGOT : 35 U/L , SGPT : 35U/L , Total bilirubin : 7 mg/dl , Direct bilirubin : 5 mg/dl , Alkaline phosphate : 720 U/L . Which of the following is the next most appropriate diagnostic step ?

- a. CT of the abdomen.
- b. Liver biopsy.
- c. Review of peripheral blood smear.
- d. Endoscopic retrograde cholangiopancreatography (ERCP)
- e. No further evaluation necessary : the patient has Dubin-Johnson syndrome.

2- Which of the following statements about achalasia is correct ?

- a. The underlying abnormality appears to be defective innervation of the esophagus and lower gastric sphincter.
- b. Dysphagia , chest pain and regurgitation are the predominant symptoms.
- c. Chest x-ray often reveal a large gastric air bubble.
- d. Manometry reveals a normal or elevated pressure of the lower gastric sphincter.
- e. Omeprazole is effective in controlling the symptoms in many patients.

- 3 - A 70 year-old woman with a history of aspirin-induced gastritis 5 years ago now has severe knee and hip pain that is thought to be due to osteoarthritis. She requires treatment with non steroidal anti-inflammatory agents, which of the following agents would be most helpful for prophylaxis against recurrent gastrointestinal bleeding ?
- Omeprazole.
 - Misoprostol.
 - Nizatidine.
 - Sucralfate.
 - Atropine.
- 4- Which one of the following diagnostic studies for malabsorption is usually normal in persons who have bacterial overgrowth syndrome ?
- Fecal fat quantitation (24h)
 - Stage II Schilling test (intrinsic factor giving with vitamin B₁₂)
 - D-Xylose absorption test.
 - Lactulose breath test.
 - Quantitative cultures of jejuna aspirates.
- 5- As a consequence of severe liver damage , hepatic amino acid handling is deranged . In this situation , plasma levels of which of the following are likely to be lower than normal ?
- Ammonia (NH₃)
 - Ammonium (NH₄)
 - Alanine.
 - Urea.
 - Glycine.
- 6- Which of the following conditions are known to predispose to the formation of cholesterol gallstone ?
- Hypertriglyceridemia.
 - Hypercholesterolemia.
 - Auto immune hemolytic anemia.
 - Sickle cell anemia.
 - Surgical resection of the ileum.

7- A patient with sclera icterus and a positive reaction for bilirubin by urine dipstick testing could have which of the following disorders ?

- a. Autoimmune hemolytic anemia.
- b. Dubin Johnson syndrome.
- c. Crigler-Najjar type II disorder.
- d. Thalassemia intermedia.
- e. Gilbert's syndrome.

8- Which of the following statements regarding delta hepatitis virus (HDV) is correct ?

- a. HDV is a defective DNA virus.
- b. HDV can infect only persons infected with hepatitis B virus (HBV).
- c. The HDV genome is partially homologous with HBV DNA.
- d. HDV infection has been found only in limited areas of the world.
- e. Simultaneous infection with HDV & HBV results in an increased risk of the development of chronic hepatitis.

9- A 55- year - old male smoker presents with burning epigastric pain several hours after a meal, which is relieved by antacids. Upper gastrointestinal endoscopy discloses an ulcer with a well-demarcated border at the duodenal bulb. Histologic examination of a biopsy specimen of the ulcer crater reveals eosinophilic necrosis with surrounding fibrosis without evidence of malignancy. Furthermore, analysis of a histologic section involving the gastric mucosa reveals invasion with a gram-negative rod. Which of the following is the most appropriate therapy?

- a. Mylanta.
- b. Ranitidine.
- c. Omeprazole.
- d. Bismuth plus metronidazole.
- e. Omeprazole plus clarithromycin plus metronidazole.

10- A 66 year-old man presents with fatigue and tea colored urine Physical examination reveals icteric sclera but is otherwise unremarkable. Which of the following conditions is LEAST likely to account for these findings ?

- a. Pancreatic cancer.
- b. Gallbladder cancer.
- c. Primary biliary cirrhosis.
- d. Auto immune hemolytic anemia.
- e. Viral hepatitis.

11- Which of the following features is more commonly associated with ulcerative colitis than with crohn's disease ?

- a. Fistulas.
- b. Rectal bleeding.
- c. Segmental involvement.
- d. An abdominal mass.
- e. Mesenteric lymph node involvement.

12 - Which of the following statements concerning the relationship of duodenal ulcer and *H. pylori* infection is correct ?

- a. Virtually all patients with a duodenal ulcer harbor *H. pylori*.
- b. Most patients infected with *H. pylori* will develop an ulcer.
- c. *H. pylori* invades the gastric mucosa.
- d. The demonstration of *H. pylori* as a causative feature in a given patient with a duodenal ulcer requires biopsy.
- e. The relapse rate for duodenal ulcer is equivalent whether *H. pylori* eradication therapy or H2 receptor antagonists are used.

13- A 56 year- old patient with cirrhosis of the liver presents with massive hemetemesis. Somatostatin, fluids and blood products are administered and the patient is intubated. Emergency endoscopy reveals bleeding esophageal varices. The patient becomes stable hemodynamically but is still bleeding. The most appropriate next step is :

- a. intravenous propranolol.
- b. intravenous vasopressin.
- c. balloon tamponade.
- d. endoscopic injection sclerotherapy.
- e. endoscopic variceal band ligation.

14- Typical causes of extra hepatic cholestatic jaundice include :

- a. sclerosing cholangitis.
- b. primary biliary cirrhosis.
- c. cystic fibrosis.
- d. alcoholic cirrhosis.
- e. non-alcoholic steatohepatitis.

15- The following features suggest extrahepatic cholestasis rather than viral hepatitis EXCEPT:

- a. a palpable gall bladder.
- b. right hypochondrial tenderness.
- c. serum alkaline phosphatase concentration >2.5 times normal.
- d. pruritus and rigors.
- e. peripheral blood polymorph leucocytosis.

16- As regard to conjugated bilirubin , which of the following is correct ?

- a. Conjugated bilirubin in the serum in hemolytic anemia is typically increased.
- b. Conjugated bilirubin in urine of healthy subjects is typically undetectable.
- c. Conjugated bilirubin normally constitutes most of the total serum bilirubin.
- d. Conjugated bilirubin in Gilbert's syndrome is typically increased.
- e. Conjugated bilirubin in the serum in obstructive jaundice is typically decreased.

17- The typical features of acute (fulminant) hepatic failure include : EXCEPT

- a. onset within 8 weeks of the initial illness.
- b. hepatosplenomegaly and ascites.
- c. encephalopathy and fetor hepaticus.
- d. nausea, vomiting and renal failure.
- e. cerebral edema without papilloedema.

18- The typical features of hepatic cirrhosis include : EXCEPT

- a. a small shrunken liver .
- b. painful splenomegaly.
- c. peripheral blood macrocytosis.
- d. parotid gland enlargement.
- e. central cyanosis.

19 - In the management of ascites due to hepatic cirrhosis :

- a. the dietary sodium intake should be restricted to 140 mmol/day.
- b. paracentesis and parenteral albumin replacement improve the survival rate.
- c. the daily calorie intake should be restricted to 1500 calories.
- d. diuretic therapy should achieve a daily weight loss of at least 2.5 kg.
- e. the protein intake should be at least 40g/day unless encephalopathy is suspected.

20 - Prevention of recurrent variceal bleeding is achievable using : EXCEPT

- a. somatostatin (*octreotide*) therapy.
- b. TIPSS.
- c. C-adrenoceptor antagonist (C-blocker) treatment.
- d. variceal banding.
- e. sclerotherapy.

21- In primary biliary cirrhosis :

- a. middle-aged males are affected predominantly.
- b. pruritus is invariably accompanied by jaundice.
- c. osteomalacia and osteoporosis both occur as the disease progresses.
- d. rigors and abdominal pain are presenting features.
- e. smooth muscle antibodies are present in high titres in the serum.

22- The typical features of primary hemochromatosis include : EXCEPT

- a. association with an autosomal recessive gene located on chromosome 6.
- b. male predominance.
- c. hepatic cirrhosis and diabetes mellitus.
- d. congestive cardiomyopathy.
- e. grey skin pigmentation due to iron deposition.

23- The typical features of pyogenic liver abscess include : EXCEPT

- a. obstructive jaundice and pruritus.
- b. tender hepatomegaly without splenomegaly.
- c. pleuritic pain and pleural effusion.
- d. multiple abscesses, especially in ascending cholangitis.
- e. Escherichia coli, anaerobes and streptococci present in pus.

24- The typical clinical features of acute cholecystitis include :

- a. jaundice, nausea and vomiting.
- b. colicky abdominal pain in spasms lasting about 5 minutes.
- c. right hypochondrial tenderness worse on expiration.
- d. air in the biliary tree on plain radiograph.
- e. peripheral blood leucocytosis.

25- As regard to viral hepatitis , which of the following is correct ?

- a. Hepatitis B can be acquired from serous fluid from a wound.
- b. Hepatitis C is not a cause of hepatocellular carcinoma.
- c. Hepatitis A is a cause of chronic liver disease.
- d. Hepatitis E can be acquired by sharing needles.
- e. A person with only a hepatitis B core IgG test positive is infectious for hepatitis B .

26- Which of the following is the most common cause of upper GI bleeding ?

- a. Mallory-Weiss tear.
- b. Variceal hemorrhage.
- c. Dieulafoy lesion.
- d. Peptic ulcer disease .
- e. Thrombocytopenia.

27- The initial regimen for a patient with tropical sprue is which of the following ?

- a. Folate and niacin.
- b. Iron sulfate and tetracycline.
- c. Gluten-free diet and prednisone.
- d. Folate and tetracycline.
- e. Azathioprine and prednisone.

28- The initial regimen for a patient with Crhon's disease is which of the following ?

- a. Folate and niacin.
- b. Iron sulfate and tetracycline.
- c. Gluten-free diet and prednisone.
- d. Folate and tetracycline.
- e. Azathioprine and prednisone.

29 - A 64-year-old man presents to his primary care physician with a complaint of foul-smelling diarrhea, which he has had for the past 4 to 5 months. He has three or four stools a day, which he describes as oily in nature. He denies experiencing a change in the caliber of his stools, and he also denies having abdominal pain, melena, or blood per rectum. His appetite is still fairly good, but he describes weight loss & fatigue. His medical history is notable for hypertension, hyperlipidemia, type 2 diabetes with retinopathy and mild neuropathy, and gastroesophageal reflux disease. His medications include metformin, insulin, atenolol, simvastatin, aspirin, and omeprazole. The neurologic examination is notable only for mild stocking-glove neuropathy, and an S₄ is heard on cardiac examination. Laboratory tests reveal macrocytic anemia and mild hypoalbuminemia.

Which of the following is the most likely diagnosis for this patient?

- a. Crohn disease.
- b. Intestinal lymphoma.
- c. Bacterial overgrowth syndrome.
- d. Hemochromatosis.
- e. Chronic pancreatitis.

30- A 75-year-old man presents with gradually worsening pruritus, jaundice, and vague right upper quadrant abdominal ache. He has a 30-year history of ulcerative colitis. On exam, he has normal vital signs, scleral icterus, and hepatomegaly. His abdominal ultrasound shows dilated intrahepatic and extrahepatic ducts but no evidence of stones. His bilirubin level is 10, alkaline phosphatase level is 400, and amylase level is normal. An abdominal CT scan finds no pancreatic masses or adenopathy.

The differential diagnosis for this patient should include which of the following?

- a. Primary biliary cirrhosis.
- b. Sclerosing cholangitis.
- c. Carcinoma of the biliary tract.
- d. Drug-induced cholestasis.
- e. B and C.

31- Which of the following is true regarding cholecystokinin ?

- a. In excess , it precipitates gallstones.
- b. It causes delayed gastric emptying through its action as a smooth muscle relaxant.
- c. It is found in higher concentrations following cholecystectomy.
- d. It releases the 'ileal brake'
- e. It stimulates pancreatic exocrine secretion.

32- Which of the following is the most effective in the treatment of gastro-esophageal reflux disease ?

- a. Ranitidine 300 mg BD.
- b. Omeprazole 20 mg OD.
- c. Bismuth TDS.
- d. Mg trisilicate .
- e. Aluminium hydroxide.

33- A 40 year old man has had mid epigastric pain and nausea for the past 2 months. On physical examination he has no abnormal findings. On upper GI endoscopy a solitary sharply demarcated 2cm shallow gastric antral ulcer is seen. Which of the following laboratory test findings is most likely to be present in this man ?

- a. Gastric achlorhydria.
- b. Positive serology for anti-nuclear antibody.
- c. Positive urea breath test.
- d. Increased plasma cortisol.
- e. Elevated serum gastrin.

34- A 28 year old woman with recent onset of a major depressive disorder ingests an entire bottle (100 capsules, 500mg each) of a medication containing acetaminophen.

Which of the following microscopic findings is most likely to be present in her liver 3 days following this ingestion ?

- a. Normal histology.
- b. Extensive necrosis.
- c. Bridging fibrosis.
- d. Severe steatosis.

35- A 30 year-old man has had a low volume, mucoid diarrhea for 3 weeks accompanied by lower abdominal pain. On examination he has no abdominal masses. His stool is positive for occult blood. Colonoscopy reveals an erythematous, friable colonic mucosa extending from the rectum to the splenic flexure. Colonic biopsies reveal mucosal ulceration with crypt abscesses. Which of the following complications is the most likely to develop?

- a. Bowel perforation.
- b. Fistula formation to the skin.
- c. Ischemic bowel necrosis.
- d. Colonic adenocarcinoma.

36- Which of the following laboratory tests is most characteristic of a patient with jaundice secondary to alcoholic hepatitis ?

- a) Ratio of AST:ALT is 3:1 and the AST is 500 U/L
- b) Ratio of AST:ALT is 2:1 and the AST is 250 U/L**
- c) Ratio of AST:ALT is 1:1 and the AST is 250 U/L
- d) Ratio of AST:ALT is 1:3 and the AST is 750 U/L

In alcoholic hepatitis, the AST:ALT ratio is usually 2:1 and the level of AST is usually < 300. When viral hepatitis or toxin induced hepatitis causes jaundice, the AST:ALT ratio is usually 1:1 and usually > 500

37- Which of the following medications causes predictable, dose dependant hepatocellular injury?

- a) Morphine
- b) INH
- c) Gold
- d) Acetaminophen**

Its daily dose shouldn't exceed 4g/d, over 15g/d will result in liver injury, >25 → fatal fulminant hepatic failure.

38- Which of the following is the most likely mechanism of paracetamol hepatotoxicity?

- a) An allergic mechanism.
- b) An active metabolite**
- c) Circulating immune mechanism
- d) A reaction with hepatic glycogen stores.

An active metabolite is hepatotoxic, It is detoxified by glutathione, & when glutathione stores are depleted, severe liver damage can occur.

39- Which of the following is the most appropriate in a case of acetaminophen toxicity?

- a) Ethanol
- b) Narcan.
- c) Cortisone
- d) N-acetylcysteine.**

It acts by binding of toxic metabolite, Narcan is effective for narcotic overdose, ethanol for methanol toxicity.

40- As regard to primary biliary cirrhosis, which of the following is most curative?

- a) Ursodiol (ursodeoxycholic acid)
- b) Methotrexate.
- c) Azathioprine.
- d) Liver transplantation.**

41- Which of the following is the most appropriate step to diagnose primary biliary cirrhosis?

- a) INR
- b) ANA
- c) Antimitochondrial antibodies
- d) CT abdomen

42- Which of the following is the most likely explanation for why early jaundice is visible in the eyes but not the skin?

- a) The high type II collagen content of the sclera tissue.
- b) The high elastin content of sclera tissue.
- c) Secretion via the lacrimal gland.
- d) The high blood flow to the head with consequent increased bilirubin delivery ☺

The sclera are high in elastin, which has an affinity for bilirubin.

43- As a consequence of severe liver damage, hepatic amino acid handling is deranged. In this situation, plasma levels of which of the following are likely to be lower than normal?

- a) Ammonia (NH_3)
- b) Ammonium (NH_4)
- c) Urea.
- d) Glycine.

Amino acids , except for the branched - chain amino acids leucine , isoleucine and valine , are taken up by the liver via the portal circulation and are metabolized to urea.

44- Which of the following conditions are known to predispose to the formation of cholesterol gallstone ?

- a) Hypertriglyceridemia.
- b) Hypercholesterolemia.
- c) Auto immune hemolytic anemia.
- d) Surgical resection of the ileum.**

Obesity, clofibrate therapy, age and oral contraceptive therapy predispose to gallstone formation by increasing biliary cholesterol excretion. Extensive ileal resection leads to malabsorption of bile salts, and an inability to micellize cholesterol. No correlation exists between serum cholesterol concentration and biliary cholesterol secretion. Other important predisposing factors to the formation of cholesterol gallstones include gallbladder hypomotility resulting from prolonged parenteral nutrition, fasting or pregnancy. Pigment gallstones may occur when the bilirubin level is high, such as in hemolytic anemia.

45- A patient with sclera icterus and a positive reaction for bilirubin by urine dipstick testing could have which of the following disorders?

- a) Autoimmune hemolytic anemia.
- b) Dubin Johnson syndrome.**
- c) Crigler-Najjar type II disorder.
- d) Gilbert's syndrome.

Under normal conditions or even in cases of unconjugated hyperbilirubinemia (e.g. hemolysis, Gilbert's & Crigler-Najjar types I and II) : the urine contains no bilirubin. This is because the unconjugated bilirubin, is tightly bound to albumin and is not filtered by the glomeruli.

- In cases of conjugated hyperbilirubinemia (e.g. Dubin Johnson, Rotor syndrome) : the urine dipstick becomes positive for bilirubin.

46- SAAG is > 1.1 g/dl in all except

- a) Tuberculous peritonitis
- b) Congestive heart failure
- c) Liver cirrhosis
- d) Budd-Chiari syndrome

47- Which of the following statements regarding delta hepatitis virus (HDV) is correct?

- a) HDV is a defective DNA virus .
- b) **HDV can infect only persons infected with hepatitis B virus (HBV)**
- c) HDV infection has been found only in limited areas of the world.
- d) Simultaneous infection with HDV & HBV results in an increased risk of the development of chronic hepatitis.

HDV is a defective virus that coinfects with and requires the helper function of HBV for its replication and expression. In general, patients with simultaneous HBV & HDV infections do not have an increased risk of developing chronic hepatitis compared with patients with acute HBV infection alone. HDV superinfection of patients with chronic HBV infection carries an increased risk of fulminant hepatitis and death.

48- A 66 year-old man presents with fatigue and tea colored urine Physical examination reveals icteric sclera but is otherwise unremarkable. Which of the following conditions is LEAST likely to account for these findings?

- a) Pancreatic cancer.
- b) Primary biliary cirrhosis.
- c) **Auto immune hemolytic anemia.**
- d) Viral hepatitis.

Bilirubin , a breakdown product of heme derived from red blood cells, is transported to the liver in an unconjugated state, which is not renally excreted.

49- Typical causes of extra hepatic cholestatic jaundice include:

- a) Primary biliary cirrhosis.
- b) Cystic fibrosis.**
- c) Alcoholic cirrhosis.
- d) non-alcoholic steatohepatitis.

- Primary biliary cirrhosis , alcoholic cirrhosis : Intrahepatic obstruction.
- Cystic fibrosis → Common bile duct obstruction from chronic pancreatitis.
- Non-alcoholic steatohepatitis : Rarely causes jaundice.

50- A 56 year- old patient with cirrhosis of the liver presents with massive hematemesis.

Somatostatin, fluids and blood products are administered and the patient is intubated.

Emergency endoscopy reveals bleeding esophageal varices. The patient becomes stable hemodynamically but is still bleeding. The most appropriate next step is :

- a) intravenous propranolol.
- b) intravenous vasopressin.
- c) endoscopic injection sclerotherapy.
- d) endoscopic variceal band ligation.**

Once bleeding develops, the first considerations are hemodynamic stabilization and airway protection. Emergency endoscopy is required to define the nature and site of bleeding.

Medical therapy with vasopressin, nitroglycerine, somatostatin or octreotide can be used to slow the bleeding while waiting endoscopy. Although endoscopic injection sclerotherapy controls the active hemorrhage in 90%, recent studies have suggested that EVL may be superior due to equal control rates with less rebleeding & fewer complications.

51- All of the following are associated with obstructive jaundice except

- a) Oral contraceptive pills
- b) Pregnancy
- c) **Criggler-Najjar type II**
- d) Secondary carcinoma of the liver

52- Which organ doesn't move with respiration

- a) **Pancreas**
- b) Liver
- c) Transverse colon
- d) Kidney

53- The following are risk factors for hepatocellular carcinoma except

- a) **Hepatic hemangioma.**
- b) Chronic hepatitis C
- c) Hemochromatosis
- d) Aflatoxin

Hemangioma is the most common benign tumor affecting the liver.

54- What do you recommend for a surgeon punctured by a needle during cholecystectomy for a patient with hepatitis C

- a) Reassurance.
- b) Active immunization
- c) Passive immunization
- d) Interferon therapy
- e) **Follow up of liver enzymes.**

There is no effective prophylaxis for HCV following exposure to infected blood. Both Ig therapy & interferon are ineffective in preventing HCV infection. There is currently no vaccine for HCV. Serial determination of anti-HCV antibodies is recommended for 6 months.

- ➡ Post exposure management for Hep B :
 - Vaccinated : no need for treatment

– Not vaccinated : IM injection of HBIG & start HBV vaccination.

☞ Post exposure risk following needlestick injuries : A C B ☺

☠ AIDS : 3 in 1000 (0.3%)

☠ Hep C : 3 in 100 (3%)

☠ Hep B : 3 in 10 (30%)

55- The following statements are true of ascites EXCEPT :

- a) **A high protein content in ascites is usual in alcoholic liver disease.**
- b) Ascites resistant to diuretics is characteristic of hepatic vein thrombosis.
- c) Ascites is sometimes associated with a pleural effusion.
- d) Ascites is a risk factor for bacterial peritonitis.

56- Which of the following is NOT dependent on bile salts for its absorption?

- a) Vitamin A.
- b) **Vitamin B.**
- c) Vitamin K.
- d) Vitamin D.

57- Which of the following drugs causes cholestatic jaundice:

- a) Rifampicin.
- b) Isoniazid.
- c) **Erythromycin.**
- d) Halothane.
- e) Paracetamol.

58- Typical features 6-8 hours after paracetamol poisoning include :

- a) Coma and ophthalmoplegia
- b) Prolongation of the prothrombin time
- c) Metabolic acidosis and hypoglycemia
- d) **Nausea, vomiting & abdominal pain.**
- ☞ Coma and ophthalmoplegia : Late features suggesting hepatic encephalopathy (after 3-5 days)
- ☞ Prolongation of the prothrombin time : Rare before 24 hours
- ☞ Metabolic acidosis and hypoglycaemia : Consequence of hepatic necrosis (after 36 hours)

59- The concentration of conjugated bilirubin in the

- a) serum in hemolytic anemia is typically increased.
- b) urine of healthy subjects is typically undetectable.**
- c) serum normally constitutes most of the total serum bilirubin.
- d) serum in Gilbert's syndrome is typically increased

As almost all bilirubin is unconjugated and albumin-bound.

60- Characteristic features of Gilbert's syndrome include EXCEPT

- a) An autosomal recessive mode of inheritance**
- b) Decreased hepatic glucuronyl transferase activity
- c) Serum bilirubin concentration increased by fasting
- d) Unconjugated hyperbilirubinemia is the sole abnormality.

Gilbert's syndrome is typically autosomal dominant.

61- The following features suggest extrahepatic cholestasis rather than viral hepatitis EXCEPT :

- a) A palpable gallbladder.
- b) Right hypochondrial tenderness**
- c) Serum alkaline phosphatase concentration > 2.5 times normal
- d) Pruritus and rigors
- e) peripheral blood polymorph leukocytosis.

Also common in acute hepatitis.

62- As regard to hepatitis C, which is correct?

- a) A chronic carriage rate of < 50% is the rule
- b) The disease does not progress to hepatoma
- c) Most patients experience the symptoms of acute hepatitis
- d) The virus is responsible for 90% of all post-transfusion hepatitis**

63- Typical liver function values in acute hepatic failure include :

- a) Hypoalbuminemia
- b) Hypoglycemia**
- c) Serum alkaline phosphatase > 6 times normal
- d) Peripheral blood lymphocytosis

Impaired hepatic gluconeogenesis.

64- The typical features of hepatic cirrhosis include EXCEPT :

- a) A small shrunken liver
- b) Painful Splenomegaly.**
- c) Peripheral blood macrocytosis.
- d) Central cyanosis

Painless Splenomegaly. Central cyanosis : Hepatopulmonary syndrome associated with pulmonary telangiectasia

65- Prevention of recurrent variceal bleeding is achievable using EXCEPT

- a) somatostatin (octreotide) therapy**
- b) TIPSS
- c) Variceal banding
- d) Sclerotherapy

Somatostatin may be useful in acute bleeds.

66- In primary biliary cirrhosis :

- a) Middle-aged males are affected predominantly
- b) Pruritus is invariably accompanied by jaundice
- c) Osteomalacia and osteoporosis both occur as the disease progresses**
- d) Smooth muscle antibodies are present in high titres in the serum.

Vitamin D malabsorption and hepatic osteodystrophy, *baby*

67- The typical features of primary hemochromatosis include EXCEPT

- a) Inherited as an autosomal recessive gene located on chromosome 6
- b) Male predominance
- c) Hepatic cirrhosis and diabetes mellitus
- d) Grey skin pigmentation due to ferritin deposition.**

Melanin not iron deposition, *baby*

68- Regarding HDV infection, which one is true?

- a) It is DNA virus
 - b) Co-infection with hepatitis B carries low risk of progression to chronic liver disease**
 - c) Super infection with hepatitis B carries low risk of progression to chronic liver disease
 - d) Can be transmitted through feco-oral route.
- HBV Co infection : Severe acute hepatitis, low risk of chronic infection.
- HBV superinfection : high risk of chronic liver disease.

69- Which of the following is correct about the anatomy of the liver?

- a) A fibrous capsule surrounds the liver lobule in humans.
- b) The hepatic vein radicles accompany the arteries in the portal tract.
- c) The liver has significant regenerative capacity.**
- d) The liver weighs around 0.5 – 1 kg in typical adults.
 - The liver has significant regenerative capacity with stem cells within the canals of Hering playing a key role.
 - It weighs 1-2 kg depending on body size.

70- Which of the following is a marker of the function of the liver in clinical use?

- a) Alanine transaminase
- b) Fibroscan
- c) Platelet count
- d) Prothrombin time**
 - Synthesis of clotting factors by the liver makes PT a useful available marker of hepatocyte function (although watch for vit K deficiency & patients on warfarin).
 - Alanine transaminase is a marker of hepatocyte injury NOT function.

71- A 63 year old man presents with yellowing of skin & sclera, Dark urine & pale stool.

He has no significant past medical history. What is the most likely diagnosis?

- a) Autoimmune hepatitis
- b) Gilbert's syndrome
- c) Hemolysis
- d) **Pancreatic carcinoma**

72- Which of the following regarding the clinical presentation and progress of paracetamol overdose is true?

- a) It has a worse outcome than acute liver failure of other etiologies
- b) If the patient recovers from acute liver failure, cirrhosis development is almost inevitable
- c) Jaundice typically occurs before PT prolongation
- d) **Pancreatitis can be a complication & typically has a very poor outcome**

The outcome of acute liver failure in paracetamol is typically better than other causes of acute liver failure. paracetamol overdose causes acute liver injury, but if the acute event is survived, the liver typically returns to normal.

73- As regard to liver transplantation, which of the following is true?

- a) Acute cellular rejection most commonly occurs between days 2 and 5
- b) At least HLA matching is essential for a good outcome
- c) **Hepatorenal failure will typically improve following liver transplantation**
- d) Immunosuppression can be safely stopped in most patients at 5 years
 - Hepatorenal failure typically improves when liver function returns to normal.
 - The most common time window for acute cellular rejection is days 7-10
 - HLA matching is unnecessary in liver transplantation (ABO blood group & weight matches in contrast are important)
 - Immunosuppression regimes differ between centers but most centers continue lifelong.

74- As regard to primary biliary cholangitis, which of the following is true?

- a) It is a different condition to primary biliary cirrhosis
 - b) It is commoner in men than in women
 - c) Patients usually show elevation of PT
 - d) The disease is more aggressive in younger patients**
 - e) Ursodeoxycholic acid (UDCA) is the first line therapy & should be used once the patient is symptomatic
- Primary biliary cholangitis is the new name for primary biliary cirrhosis
 - It is 10 times commoner in women than men.
 - UDCA is first line therapy & should be used in all patients regardless of symptoms status.
 - The most characteristic blood test is elevation of **Alkaline phosphatase**.
 - **PT**, bilirubin and albumin tend to be **normal** until late in the disease.

75- A patient with primary biliary cholangitis is concerned about the prognosis of her disease. Which of the following is predictive of a poor control?

- a) Alkaline phosphatase (ALP)**
 - b) AMA titre
 - c) Older age at disease onset
 - d) Large liver size on US
- AMA is an important diagnostic feature but titre is not predictive of outcome.
 - Liver size is typically increased in early PBC. Small size is a feature of cirrhosis with a worse outcome
 - Younger age is associated with a lower likelihood of response to UDCA and increased risk. PBC is typically benign in older patients.

76- A 22 year old man with no significant past history presents with a 1 week history of acute lethargy and jaundice 2 weeks after returning from a week long holiday in Turkey. His alanine aminotransferase (ALT) is found to be over 10000 U/L. what is the most likely diagnosis?

- a) Alcoholic hepatitis
- b) Hepatitis B
- c) Hepatitis C

d) Hepatitis E

- The clinical scenario is strongly suggestive of an acute viral hepatitis and the timing of onset would be most compatible with HEV. The onset in HBV is much more prolonged, although clearly infection prior to the holiday in Turkey is possible.
- HCV almost exclusively cause chronic liver injury with no recognized acute infection event.
- Alcohol hepatitis in this case is very unlikely, as ALT of 10000 U/L would be very atypical.

77- A 25 year old female with well controlled, non-cirrhotic autoimmune hepatitis attends your clinic to say she is pregnant. She is currently maintained on azathioprine monotherapy. What advice would you give her?

a) Disease flare-ups can occur following delivery

- b) Her child runs a significant risk of developing AIH
- c) Her disease will deteriorate during pregnancy
- d) She should undergo endoscopy
- AIH typically improves during pregnancy. It can however flare up during the early post-partum period.
- If patients have cirrhosis, then portal hypertension can worsen during the 3rd trimester, so endoscopy should be considered as they enter the 3rd trimester. This only applies to cirrhosis patients.
- The offspring of mothers with AIH run a slightly increased risk of AIH later in life because of the genetic factor). But this small risk should not impact on plans for pregnancy.

78- Which of the following is the most common symptom or sign of liver disease?

a) Fatigue**b) Itching****c) Jaundice****d) Right upper quadrant pain****e) Nausea**

79- A 53 year old man with known esophageal varices presents with a large GI bleed. You are the first attending clinician. What is the first step you should take?

- a) Urgent cross match
 - b) Urgent endoscopy and banding
 - c) Insert large bore cannula and give fluid**
 - d) Ultrasound to assess for portal vein thrombosis
- Here it is essential to secure venous access early & commence fluid resuscitation.
 - Cross matching is clearly urgent but should be done once access is secured.
 - The acute intervention of choice is endoscopy and banding but this should only be undertaken once the patient is hemodynamically stable.

80- A patient with suspected variceal bleeding cannot have an endoscopy because of lack of an available trained endoscopist. She is becoming increasingly unstable. Which of the following is a first medical therapy of choice for use to establish hemodynamic control?

- a) Glypressin**
 - b) Noradrenaline
 - c) Propranolol
 - d) Subcutaneous octreotide
- Glypressin is recognized to reduce the severity of acute variceal bleeding and can act as a bridge to endoscopy.
 - Noradrenalin may be required to maintain cardiovascular status but not to reduce bleeding risk.
 - Propranolol should **never** be used in acute bleeding but is an important agent in the treatment of chronic portal hypertension.
 - Octreotide has been superseded by Glypressin: where used, it has to be intravenous.

81- which of the following viral causes of acute hepatitis is most likely to cause fulminant hepatitis in a pregnant female?

- a) Hepatitis A
- b) Hepatitis B
- c) Hepatitis C
- d) Hepatitis D
- e) Hepatitis E**

82- A CT scan performed in the patient with chronic liver disease has identified a mass lesion suspicious of a hepatocellular carcinoma. What is the next investigation you should consider?

- a) MRI scan
- b) Blood alpha fetoprotein (AFP) measurement
- c) Laparoscopy
- d) Liver biopsy
- e) Positron emission tomography (PET) scan
 - AFP has some use as a screening test in at risk patients but it can be normal in patients with HCC.
 - Laparoscopy & liver biopsy can be used in staging & planning therapy in specific cases once the diagnosis is supported by imaging.
 - PET scan is used in particular to explore for the presence of metastasis.

83- A 45 year old female presents with painful hepatomegaly and ascites. What imaging finding would you predict?

- a) An irregular liver on CT
- b) Hepatic artery thrombosis
- c) **Hepatic venous thrombosis**
- d) Isolated gastric varices
 - The clinical presentation is typical of Budd Chiari syndrome (hepatic venous thrombosis). Cirrhosis is typically associated with a small painless shrunken liver.
 - Hepatic artery thrombosis is a specific complication of liver transplantation.

84- An otherwise healthy 35 year old nurse is referred with a persistent fluctuating transaminitis (ALT 40-120 U/L) that has been present for several years. What viral infection would you consider most likely?

- a) Hepatitis A
- b) Hepatitis B
- c) **Hepatitis C**
- d) Hepatitis E

- Notice that health workers are routinely immunized against HBV, making chronic HBV less likely.
- Acute symptomatic infection with HCV is rare & most individuals are unaware of when they became infected & are only identified when they develop chronic liver disease.

85- twenty four hours following liver transplantation for autoimmune hepatitis, a patient's ALT is climbing rapidly. What diagnosis is the most likely?

- a) Acute cellular rejection
- b) CMV infection
- c) Hepatic artery thrombosis**
- d) Recurrent AIH

86- A 38 year old man is referred to the outpatient clinic. His father had hemochromatosis. He is wondering whether he is likely to be affected. What would be the best first line screening test in this case?

- a) CT liver
- b) Ferritin
- c) Genetic analysis
- d) Liver biopsy
- e) Transferrin saturation**

Transferrin saturation of more than 45% is highly suggestive of iron overload & not affected by inflammatory state and so is more specific than ferritin.

87- Elevation in all of the following laboratory studies would be indicative of liver disease EXCEPT

- a) 5'-nucleotidase
- b) Aspartate aminotransferase
- c) Conjugated bilirubin
- d) Unconjugated bilirubin**
- e) Urine bilirubin

Isolated elevation in the unconjugated bilirubin is typically not related to liver disease but is most commonly seen in hemolysis and a number of benign genetic conditions such as Gilbert syndrome.

88- Which of the following tests would be LEAST likely to be positive in autoimmune hepatitis?

- a) ANA
- b) Anti-liver/kidney microsomal antibodies
- c) **Antimitochondrial antibodies**
- d) Hypergammaglobulinemia

Antimitochondrial antibodies are typically seen in primary biliary cirrhosis.

89- As regard to NAFLD, all of the following statements are true EXCEPT

- a) NAFLD is strongly associated with obesity & insulin resistance
- b) NAFLD can occur in lean individuals
- c) Exercise may reduce hepatic steatosis
- d) **Statins may worsen inflammation in NAFLD**
- e) There are no Food and Drug administration approved therapies for NAFLD

90- In the patient with acute variceal hemorrhage, management includes all EXCEPT

- a) Endoscopic sclerotherapy
- b) Endoscopic band ligation
- c) Octreotide
- d) **Propranolol**
- e) TIPS

91- In a patient with cirrhosis, all of the following findings are suggestive of the development of portal hypertension EXCEPT

- a) 15 mmHg gradient between wedged and free hepatic vein pressures
 - b) Ascites on ultrasound
 - c) Enlarged spleen on physical examination
 - d) **Left atrial dilatation on echocardiogram**
 - e) Thrombocytopenia
- Normal wedged to free gradient (which is equivalent to the portal pressure) is 5 mmHg, & patients with gradient > 12 mmHg are at risk of variceal hemorrhage.
 - Dilatation of right atrium (NOT left) may be found in cardiac cirrhosis

92- A 42 year old man with cirrhosis related to hepatitis C has ascites requiring frequent large volume paracentesis. All of the following therapies would be indicated for this patient EXCEPT

- a) Fluid restriction to less than 2 L daily
- b) Furosemide 40 mg daily
- c) Sodium restriction to less than 2 g daily
- d) Spironolactone 200 mg daily
- e) TIPS if medical therapy fails

93- All of the following are potential indications for liver transplantation EXCEPT

- a) Autoimmune hepatitis
- b) **Cholangiocarcinoma**
- c) Primary biliary cirrhosis
- d) Primary hepatocellular carcinoma

Patients with cholangiocarcinoma (bile duct cancer) are not transplantation candidates because of high rate of recurrence.

94- What laboratory test (s) should be ordered to screen for acute hepatitis B infection?

- a) Anti-HBe
- b) HBsAg and anti-HBs
- c) **HBsAg and IgM anti-HBc**
- d) HBeAg

95- Which of the following laboratory findings do you expect in a patient with hepatolenticular degeneration?

- a) Elevated serum ferritin
- b) Elevated serum copper
- c) **Decreased serum ceruloplasmin**
- d) Decreased urinary copper

Answers

1- a. CT of the abdomen.

Initial considerations in evaluating a patient with jaundice require a determination of whether the patient has primarily unconjugated hyperbilirubinemia or conjugated hyperbilirubinemia, in which case > 50 % of the serum bilirubin is conjugated bilirubin. The major differential diagnosis in this case is between impaired hepatocyte bilirubin excretion and extrahepatic biliary obstruction. Intra hepatic obstruction may occur in drug reactions, alcoholic hepatitis, the third trimester of pregnancy and viral or autoimmune hepatitis. In the case of Dubin-Johnson syndrome, the conjugated hyperbilirubinemia is due to a congenital defect in bilirubin excretion and generally is not associated with abnormalities of alkaline phosphatase or hepatic amino-transferases. Patients who have conjugated hyperbilirubinemia and abnormal liver enzymes generally fall into two groups: those whose aminotransferase elevation is dominant and who are suspected of having a hepatocellular disorder and those who have primary elevation of alkaline phosphatase and are likely to have either intra or extra hepatic biliary obstruction. In the latter group of patients, it is imperative to rule out extra hepatic obstruction by means of ultrasonography of the right upper quadrant or abdominal CT. If the biliary ducts are not dilated on radiologic evaluation, the next most appropriate procedure would be ERCP.

2- b. Dysphagia, chest pain and regurgitation are the predominant symptoms.

Achalasia is a motor disorder of esophageal smooth muscle in which the lower esophageal sphincter (LES) does not relax properly in response to swallowing and normal esophageal peristalsis is replaced by abnormal contractions. Manometry reveals a normal or elevated LES pressure and reduced or absent swallow-induced relaxation. A decreased number of ganglion cells are noted in the esophageal body and LES of patients with achalasia, suggesting that defective innervations of these areas is the underlying abnormality. Dysphagia, chest pain and regurgitation are the predominant symptoms. The chest x-ray often reveals absence of the gastric air bubble, and the barium swallow reveals a dilated esophagus. Calcium channel antagonists such as nifedipine relax smooth muscle and have been effective in treating some patients. However, the mainstay of therapy remains pneumatic dilation.

3- b. Misoprostol.

Gastric mucosal injury, potentially resulting in ulcers and erosive gastritis, may be produced by aspirin and nonsteroidal anti-inflammatory drugs including indomethacin, ibuprofen and naproxen. These agents may be directly toxic to the gastric mucosa by depleting protective endogenous mucosal prostaglandins. Moreover, they more directly interrupt the mucosal barrier, allowing back diffusion of hydrogen ions as well as reducing gastric mucus secretion and increasing gastric acid secretion. The prostaglandin E analogue misoprostol is effective in preventing ulcers and gastritis caused by NSAIDs. Its mechanism of action is believed to be stimulation of gastric mucus and duodenal bicarbonate secretion as well as the maintenance of the gastric mucosal barrier via epithelial cell restitution.

4- C. D-Xylose absorption test.

Malabsorption caused by bacterial overgrowth results from bacterial utilization of ingested vitamins and the deconjugation of bile salts by bacteria in the proximal jejunum . The bacteria also separate vitamin B 12 from the intrinsic factor, thus interfering with its absorption from the ileum. persons with bacterial overgrowth have steatorrhea , an abnormal Schilling test (even with the administration of intrinsic factor), increased metabolism of non absorbable carbohydrates (lactulose) and increased bacterial concentrations in jejunal aspirates. Absorption of D- Xylose , a simple carbohydrate , is often normal.

5- D. Urea.

Amino acids , except for the branched - chain amino acids leucine , isoleucine and valine , are taken up by the liver via the portal circulation and are metabolized to urea .

6- E. Surgical resection of the ileum.

Obesity , clofibrate therapy , age and oral contraceptive therapy predispose to gallstone formation by increasing biliary cholesterol excretion . Extensive ileal resection leads to malabsorption of bile salts , depletion of the bile acid pool , and an inability to micellize cholesterol , resulting in an increased risk of gallstone formation. No correlation exists between serum cholesterol concentration and biliary cholesterol secretion . Hypercholesterolemia does not predispose to cholelithiasis. Other important predisposing factors to the formation of cholesterol gallstones include gallbladder hypomotility resulting from prolonged parenteral nutrition , fasting or pregnancy. Pigment gallstones may occur when the bilirubin level is high , such as in hemoglobinopathies or hemolytic anemia.

7- B. Dubin Johnson syndrome.

- Under normal conditions or even in cases of unconjugated hyperbilirubinemia (e.g. hemolysis, Gilbert's & Crigler-Najjar types I and II) : *the urine contains no bilirubin. This is because the unconjugated bilirubin , is tightly bound to albumin and is not filtered by the glomeruli.*
- In cases of conjugated hyperbilirubinemia (e.g. Dubin Johnson , Rotor syndrome) : the urine dipstick becomes positive for bilirubin.

8- B. HDV can infect only persons infected with hepatitis B virus (HBV).

HDV is a defective virus that coinfects with and requires the helper function of HBV for its replication and expression. Therefore, the duration of HDV infection is determined by and limited to the duration of HBV infection. Although the delta core is encapsulated by an outer coat of HBsAg, the delta antigen has no antigenic similarity to that of any of the HBV antigens. In general, patients with simultaneous HBV & HDV infections do not have an increased risk of developing chronic hepatitis compared with patients with acute HBV infection alone. HDV superinfection of patients with chronic HBV infection carries an increased risk of fulminant hepatitis and death.

9- E. Omeprazole plus clarithromycin plus metronidazole.

This patient has the classic clinical symptoms and endoscopic findings of a duodenal ulcer. It is now a recommendation that *H. pylori* infection should be eradicated in patients with documented peptic ulcer disease. No single or double agent regimen has been reliably effective in eradicating the organism. In general, a combination of two antibiotics plus a proton pump inhibitor (*omeprazole*) is required to achieve a high likelihood of eradication. Such triple therapy is effective in eradicating the organism in approximately 90 % of the cases.

10 - D. Auto immune hemolytic anemia.

Bilirubin, a breakdown product of heme derived from red blood cells, is transported to the liver in an unconjugated state, which is not renally excreted. The conjugation of bilirubin occurs in the endoplasmic reticulum of the hepatocyte when the molecule is attached to glucuronic acid. The conjugated bilirubin is then transported into the bile, then into the colon where most is excreted into the feces. Processes that prevent excretion of conjugated bilirubin due to intra hepatic diseases e.g. viral hepatitis, drugs as estrogen, chlorpromazine, or extra hepatic obstruction (blockage due to cancer of the biliary system or pancreas, bile duct diseases such as sclerosing cholangitis, primary biliary cirrhosis lead to an increase of this species in the blood. Elevated levels of this soluble form of bilirubin can be detected visually as tea or cola-colored urine. Ultrasonography, CT or ERCP would be necessary to distinguish between extra and intra hepatic causes of conjugated - hyperbilirubinemia. Unincreased load of unconjugated bilirubin produced in states of excessive red cell destruction would generally not be detected in a urine test for bilirubin.

11- B. Rectal bleeding.

There are many similar manifestations of Crohn's disease (CD) and ulcerative colitis (UC). However UC almost always displays continuous rather than the more segmental involvement characteristic of CD. UC rarely involves the entire bowel wall, whereas such transmural disease in CD can lead to abdominal masses, mesenteric node inflammation, and fistula formation. Since CD is much less likely to involve the rectum, hematochezia is less common than it is in UC. Extra intestinal manifestations, colonic malignancy and toxic megacolon can occur with either entity.

12- A. Virtually all patients with a duodenal ulcer harbor *H. pylori*.

Although only 15 - 20% of persons infected with the spiral shaped, gram negative bacillus *H. pylori* will develop an ulcer 95 - 100% of those with a documented duodenal ulcer can be shown to have *H. pylori* infection. Typically the organism is found in the deep portion of the mucus gel. Although bacteria may adhere to the luminal surfaces of the gastric epithelial cells, they do not invade the mucosa. It appears that the bacteria activate inflammatory cells that produce mucosal damage and release enzymes such as proteases and phospholipases which degrade the mucus gel layer. The prevalence of gastric colonization with *H. pylori* increases with age and with lower socioeconomic status. There are multiple ways to diagnose *H. pylori* infection including histologic examination, culture measurement of urease activity and serologic studies. The most effective way to decrease the relapse rate for duodenal ulcer is to institute therapy that successfully eradicates *H. pylori*. The relapse rate is much higher if H₂ receptor antagonists are used alone.

13- E. endoscopic variceal band ligation.

One of the most important complications of hepatic cirrhosis is variceal bleeding, which along with ascites and encephalopathy results from portal hypertension. The primary prophylaxis of known or previously bleeding varices includes cessation of alcohol, beta blockers, nitrates and possibly endoscopic variceal band ligation (EVL). Once bleeding develops, the first considerations are hemodynamic stabilization and airway protection. Emergency endoscopy is required to define the nature and site of bleeding. Medical therapy with vasopressin, with or without nitroglycerine or with somatostatin or octreotide can be used to slow the bleeding while awaiting endoscopy. Although endoscopic injection sclerotherapy controls the active hemorrhage in 90%, recent studies have suggested that EVL may be superior due to equal control rates with less rebleeding, fewer complications and reduced number of sessions. Balloon tamponade can be used if clinical stability can not be achieved and endoscopy is not immediately available.

14- C. cystic fibrosis.

- Sclerosing cholangitis, primary biliary cirrhosis, alcoholic cirrhosis : Intrahepatic obstruction.
- Cystic fibrosis : Common bile duct obstruction from chronic pancreatitis.
- Non-alcoholic steatohepatitis : Rarely causes jaundice.

15- B. right hypochondrial tenderness.

Right hypochondrial tenderness : Also common in acute hepatitis.

16- B. Conjugated bilirubin in urine of healthy subjects is typically undetectable.

- o As almost all bilirubin is unconjugated and albumin-bound.
- o In hemolytic anemia, there is unconjugated hyperbilirubinaemia.
- o Unconjugated bilirubin is increased in Gilbert's syndrome.
- o Conjugated bilirubin in the serum in obstructive jaundice is typically increased.

17- B. hepatosplenomegaly and ascites.**18- B. painful splenomegaly.****19- E. the protein intake should be at least 40g/day unless encephalopathy is suspected.**

- o The dietary sodium intake should be restricted to < 40 mmol/day.
- o paracentesis and parenteral albumin replacement are symptomatic measures with no prognostic value.
- o Calorie restriction is neither required nor desirable.
- o Daily weight loss >1 kg may precipitate renal impairment and/or encephalopathy.
- o Protein restriction may be necessary to control encephalopathy.

20- A. somatostatin (octreotide) therapy. Somatostatin may be useful in acute bleeds.

21- C. osteomalacia and osteoporosis both occur as the disease progresses.

- middle-aged females are affected predominantly.
- pruritus may precede jaundice by months or even years.
- osteomalacia and osteoporosis both occur as the disease progresses due to Vitamin D malabsorption and hepatic osteodystrophy.
- rigors and abdominal pain are presenting features suggest obstruction of large bile duct.
- High titres of anti mitochondrial antibody , not smooth muscle antibodies.

22 - E. grey skin pigmentation due to iron deposition.

Melanin not iron deposition.

23 - A. obstructive jaundice and pruritus.

Jaundice is usually mild and not often obstructive.

24 - E. peripheral blood leucocytosis.

- Jaundice occurs in less than 20% even in the absence of stones (*Mirizzi's syndrome*)
- Pain is typically continuous for up to 6 hours.
- right hypochondrial tenderness worse on inspiration (*Murphy's sign*).

25 - A. Hepatitis B can be acquired from serous fluid from a wound.**26- D. peptic ulcer disease.****27- D. Folate and tetracycline.****28- E. Azathioprine and prednisone.****29- B. Bacterial overgrowth syndrome.**

This patient has a subacute to chronic presentation with steatorrhea and likely folate deficiency, vitamin B₁₂ deficiency or both. He has diabetes mellitus, which can cause stasis through autonomic neuropathy. Anything that causes intestinal stasis allows a proliferation of bacteria, which leads to changes in bile salt metabolism and impaired absorption, primarily of vitamin B₁₂ . In addition , this patient is taking proton pump inhibitor , which can reduce motility of the proximal small bowel, often precipitating symptoms in a predisposed patient. Therapy usually entails repeated courses of antibiotics active against anaerobes. There is no convincing evidence for the effectiveness of any of the other choices presented.

30- E. B and C.

In this case, other possible diagnoses include a solitary common bile duct stone that escaped detection on ultrasound and CT, occult pancreatic carcinoma, bile duct stricture, and extrahepatic compression of the biliary tract. Although sclerosing cholangitis usually develops in younger men (aged 20 to 50 years), it is often associated with ulcerative colitis. About 60% of patients will also have a positive perinuclear antineutrophil cytoplasmic antibody (p-ANCA) test result. The hallmark finding on ERCP is segmental stenosis of the biliary tree. Primary biliary cirrhosis is an autoimmune disease that typically affects women. About 95% of patients have antimitochondrial antibodies. Both primary biliary cirrhosis and drug-induced cholestasis cause intrahepatic cholestasis without extrahepatic duct dilatation.

31- E. It stimulates pancreatic exocrine secretion.

32- B. Omeprazole 20 mg OD.

33- C

H.Pylori organisms produce urease enzyme which will break down urea to ammonia & CO₂. The patient drinks a measured quantity of a urea containing solution with radiolabelled carbon. If the H.Pylori organisms are present they metabolize the urea and release the radiolabelled carbon which is detected in exhaled air. Most gastric ulcers of this size are benign.

34- B Massive overdose of acetaminophen → causes extensive hepatic necrosis.

35- D Chronic ulcerative colitis carries a significant risk for development of colonic adenocarcinoma 2-3 decades after onset.

36 – 95: done before

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